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The Causes and effects of obesity with special reference to complications and sequelae

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THE CAUSES AND EFFECTS OF OBESITY

With Special Reference To Complications And Sequelae

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INTRODUCTION

The purpose of this paper is a consideration of obesity from the standpoint of its etiology and complications. The former will receive slightly less attention because of the already voluminous treatment of this phase of the subject in the literature. It's importance is such , however, that for the sake of properly evaluating the manner in which obesity operates as a factor in other diseases, it cannot be considered too briefly. Special emphasis will be directed toward as much as is known concerning the mechanism by which obesity predisposes or causes conditions commonly associated with it.

Although the title implies a distinction between the meaning of complications and sequelae, no attempt well be made to differentiate these terms. Complication is usually applied to concurrent disease, whereas sequela is used to designate any affection which follows and occurs as a result of the primary condition. In as much as nearly all associated conditions are concurrent with the obesity and may at the same time be directly or indirectly a result of it, it is obvious that no sharp distinction between them is practicable. Uncer-

tainty with regard to the exact role of obesity in certain of its coincident diseases obviates the neeessity of regarding these terms as more or less synonymous. As the succeeding evidence is presented the justification for disregarding any distinction will be apparent. This is unfortunate, but at the same time the principal reason for the writer's interest in this phase of the subject.

The author knows of no other paper in which a correlation of the many facts which have been established in regard to obesity as an etiologic factor in other diseases has been attempted. It is true that many papers have been written concerning obesity and its attendent complicating pathology, but in general these have not attempted a comparison of experimental evidence from other investigators to establish any conclusions which are made. Those contributors with experimental evidence to support their conclusions, have in the main considered only one of the host of complicating conditions which has been ascribed to obesity by the earlier writers. Both etiology and treatment of obesity as well as its endocrinopathy, have received the bulk of consideration in articles appearing on this subject in the past. While these are important, the author feels that more emphasis should

be placed on the complications or sequelae in order that the practicing physician may give more careful consideration to the prophylaxis or prevention of a disease which produces so much morbidity and mortality. It is with these facts in mind, together with the absence of a similar treatise in the literature which motivates the preparation of this paper.

In outlining the scope of the present work it is the author's intention to present a short chapter on the definition, historical incidence, and statistical significance of obesity before undertaking a discussion of its causes and effects. This is imperative if a better understanding of obesity as a predisposing factor in other disease is to be gained. The considerations of classification and endocrinology cannot be entirely excluded from the discussion of the etiology. Symptoms and prognosis will be mentioned in the chapter on complicating pathology. Methods of treatment will receive the least emphasis since these are constantly changing as newer concepts of the pathogenesis are advanced. Wherever appropriate, however, certain principles of therapy will be included. It is hoped that these apparent omissions may not be construed to minimize their importance, nor detract from the interest in a discussion of etiol-

ogy and complications.

In regard to the complications or sequelae it is also obvious that a complete survey of all the diseases in which obesity has been suggested as a contributing factor, is impossible, though the author hopes at least to mention most of them, reserving the bulk of such considerations to only the more important complications. It is true that all contributors in this field cannot be mentioned and the author purports to present only the more important contributions which have appeared in the last two decades. Although many of the contributions have added to a knowledge of the subject during this time, no chronological mode of presentation will be necessarily followed.

The present work represents a review of literary material only. Much of this was selected from the Quarterly Cummulative Index Medicus of the American Medical Association from 1916 to date, and to a lesser extent from other reference lists and bibliographies selected at random and during the work of preparation. Numerous books on the subject were also consulted in a further attempt to make as complete a survey as time would permit. The bibliography includes only such references as were available from the Library of the College of Med-

icine, University of Nebraska, Omaha. Much of the literature in foreign language was necessarily excluded because of inability to translate it, though wherever possible abstracts and translations were used, the source or translator being indicated parenthetically following the reference in the bibliography. Footnotes will be used to indicate the source of citations used which have been made by various authors, but which have not actually been reviewed by the author. In this way the bibliography comprises only such material as was directly consulted.

Before commencing with the discussion of the subject, a review of the present concept of the role played by normal fat in the human organism is included.

The author wishes to express appreciation to the librarian and her staff for their kind assistance in finding many of the references, and to Dr. Lowell F. Dunn for his helpful advice and suggestions.

NORMAL FAT IN THE HUMAN BODY

The source of fat in the human body is from the food we eat. Grafe (46) says that it is the most perfect foodstuff in that except for its chief function, which is to be burned and thus to provide energy, it is largely deposited unchanged in our bodies. E.F. DuBois (36) states that fats furnish about one-third of our caloric intake in health. He also points out that carbohydrates may be converted into fat in the body, this conversion being an exothermic reaction because the change from an oxygen-rich to an oxygen-poor compound occurs. This raises the respiratory quotient because but little oxygen absorption is required from the outside. Lambie (66) states that this conversion can take place by the condensation of three molecules of glucose to form fatty acid which unites with glycerol to form fat. He emphasizes the fact that body or depot fat is derived from all three foodstuffs, but that because carbohydrate comprises two-thirds of the average caloric intake, most of it comes from this foodstuff. He states that protein normally becomes fat only to a small extent from the inter-

mediary protein metabolism of glutogenic amino acids which are changed to the carbohydrate form of triose and thence to fat as above, but that condensation of triose to form hexose is less readily accomplished than its conversion into glycogen from which glucose and fatty acid would be formed. DuBois (36) however, says that there is but little evidence to show that proteins are converted to fat, but points out that theoretically since about one-half the protein is metabolised as glucose, this much may become fat. He states that the mechanism of the digestion, absorption, and metabolism of fats is not known with certainty. Grafe (46) states that carbohydrate may be transformed to fat in the depots themselves, and is second in importance as a source of fat, proteins coming next and finally alcohol, but adds that fat is the real fattening and reserve substance. DuBois (36) points out that the edible simple lipoids are esters of the triatomic alcohol, glycerol, which consist of mixtures of tristearin, tripalmitin, and triolein. Bloor (20) states that other ingested complicated lipoids include the phospholipids mainly.

The digestion of simple or neutral fat is stated by Bloor (20) to commence in the stomach through the action of gastric lipase, provided the acidity is low and the

emulsification sufficient. He points out that although fat inhibits the acid and slows the passage of food into the intestine, emulsion such as milk or oils leave the stomach rather rapidly. In the intestine conditions are most ideal for fat digestion where the alkaline secretions of pancreatic juice, intestinal secretion, and bile all take place. The intestinal and pancreatic juices each furnish a lipase which hydrolyzes the fat with the assistance of bile, which not only renders the enzyme more active, but increases the solubility of the fatty acids produced in the hydrolysis, which in part unite with the alkalies to form soaps, both assisting in the emulsion of the rest of the fat. He states that fats are probably absorbable only in water-soluble form and intimates that the complicated lipoids as the phospholipid, lecithin, and cholesterol may be absorbed readily because they are soluble and easily hydrolyzed. He believes that water solubility is the test applied by the organism to all ingested fats before absorption by the intestine and protects it against the assimilation of useless fats. DuBois (36) states that as a rule fats with low melting points are better assimilated than those which do not melt at body temperature.

Bloor (20) states that fat excreted in the feces

is comprised of three form: Undigestible fat, fat from cellular and bacterial debris, and true intestinal excretion of unusable fat. He points out that in fasting one-third of the total dry matter of the feces is fat, and, as further evidence that the intestine actually excreted fat, indicates that there is sometimes more fat in the feces than in the food. He says that there is normally a trace of fatty acid in the urine. DuBois (36) also states that the intestine excretes fatty substances in small amounts, even during starvation. He cites Atwater[1] as reckoning a loss in the excreta of 5% of animal fat and 10% of the vegetable fat ingested.

The mechanism of absorption of fat is not definitely worked out, but Maximow (77) states that during the absorption of fat, the striated border and subjacent homogeneous protoplasmic layer of the intestinal epithelium always remains free of fat droplets. He says fat droplets appear above the Golgi net and the nucleus of the cell which proves that the invisible glycerol and fatty acids are at least in part immediately resynthesized by the cell into neutral fat. He points out that some investigators have seen droplets between the basal

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1. Atwater and Bryant, Report of the Storrs (Conn.) Exper. Station, p. 73, 1899.

parts of epithelial cells, while others claim that the leucocytes transfer fat from the cells into the lacteals, but adds that this is probably not correct. Bloor (20) also states that the fatty acids and soaps are absorbed only to be resynthesized with glycerol to form neutral fat in the wall of the gut again, whence it reaches the blood stream by way of the lacteals and thoracic duct mainly, but to a lesser extent may go directly into the portal circulation. He says that the suspension of minute particles of resynthesized neutral fat in the blood causes a slight milkiness of the plasma which may persist 8-14 hours after the fat meal and that persistance for 14 hours after a meal indicates an abnormality in fat metabolism.

Bloor (20) points out that the extent and duration of the increase of blood fat following a fat meal, depends on the amount of fat ingested and also apparently on the level of the blood lipoids at the time of feeding, because if high the fall is slower than when the level of blood lipoids is low. He states that coincident with the rise of neutral fat in the blood during fat absorption, certain changes in the other blood lipoids have been observed. He says that with a rise in blood fat, the phospholipid, lecithin is the first to increase and later cholesterol, the order of the increase being an explana-

tion why some workers get no increase in the latter after a fat meal, since the amount ingested is too small to stimulate the rise of the third blood lipoid, cholesterol. Rony and Levey (105) found that following ingestion of one pint of 20% cream, an increase of the fatty acid content of the blood occurred, the peak of the curve being reached in from 3-5 hours in normal individuals, but observed no change in the plasma cholesterin in these same subjects. Apparently their result is explained by Bloor (20) above, who states further, that the mechanism of the disappearance of fat from the blood is uncertain, but is found to accumulate in the liver, bone marrow, spleen, and muscles, in the order named.

Joslin (59) states that the normal range of cholesterol in the blood varies between the lowest fasting level of 125 to the highest level of 230 mg./100 cc., reached in 3-4 hours after a meal, the amount varying directly with the amount of total fat in the blood. Bruger and Poindexter (24) found the blood cholesterol in normal subjects to range between 160-230 or 250 mg./100 cc., when taken in the morning after breakfast. Musser (87) points out that since the rate of digestion and absorption of fat is uniform, the alimentary lipemia

curves may be used as approximate measures of the rate of fat utilization, but Stewart, Gaddie, and Dunlop (111) could find no relationship between utilization of fat and changes in the blood fat concentration in normal subjects fed on nothing but carbohydrates and fats, the latter given in increasing amounts. They furthermore did not find any figures to suggest any conversion of fat to carbohydrate, but found that low blood fat was increased by work while high blood fat was decreased after work so that fat was directly oxidized, and suggested that extra amounts of fat in the blood were derived from adipose tissue. These rather conflicting views are undoubtedly dependent on the present incomplete knowledge of the actual mechnism of fat utilization by the tissues.

Bloor (20) states that lipases are found only in the pancreas and intestine and are the only enzymes capable of hydrolyzing the fats of the higher fatty acids which are the type ordinarily ingested as food. Hence resynthesized neutral fat in the blood stream cannot be hydrolyzed by the tissues without undergoing some change, and he believes that because of the coincident rise of lecithin and cholesterol with fat in the blood after a meal, these substances must therefore take part in the

metabolism of fat. He states that cholesterol is in constant relation with its fatty acid esters and Musser (87) points out that the relation of the cholesterol esters to the cholesterol in the blood may be a more important measure of liver changes because the former do not pass through the liver cells normally as does cholesterol. Bloor (20) further states that the esterases are widespread throughout the blood and tissues of the body, but are capable of hydrolyzing only the shorter chain fatty acids and the phospholipids as lecithin, the latter therefore being the most likely form in which fat can be utilized by the tissues. He believes that since the blood corpuscles have also been shown to contain an increase in fat and lecithin content during fat absorption that a transformation of fat into lecithin probably takes place, a process seemingly likely because of the increase of the latter after fat ingestion. In some animals where the lecithin does not increase in the corpuscles he explains that its formation could be followed by immediate release into the plasma. He adds that the evident interdependence of fat, lecithin, and cholesterol in the blood is proof of their role in the metabolism of the fatty acids.

Bloor (20) believes, since the liver is the

only organ loaded with fat during absorption of this foodstuff and the fatty acids of this fat are found to be of the same degree of saturation as those of the food fat by determination of the iodine number, that this organ is the site of the desaturation of the neutral fat of the blood. Evidence for this is found in the analysis of tissue fat, which he states is a complex cellular lipoid built into the active tissues of the body and is comprised mainly of phospholipids, which are the most widely distributed, but also cholesterol and other known complex lipoids. In contradistinction to the depot fat, he adds that the active tissue lipoids having an iodine number of 35-70 are highly desaturated, whereas the former is of the same degree saturation as ingested fat, whose fatty acids have an iodine number of around 130. Hence it would appear that for utilization by the tissues, the more highly active desaturated form of fatty acids is necessary, as well as phosphorization, in which process the liver seems to be the most probable site since the same process may occur in the corpuscles and tissues. Musser (87) states that active white blood cells have a high phospholipid and low cholesterol ester content, while inactive or degenerating cells show the reverse relationship.

It has long been believed, as pointed out by Maximow (77), that cholesterol arises from the stroma of old red blood cells and is excreted by the hepatic cells into the bile, whereas the bile acids are manufactured and secreted by these same liver cells. Corresponding to Bloor's (20) active tissue complex cellular lipoid, Maximow also describes a masked or bound fat which is part of living protoplasm and is difficult to demonstrate microscopically, but may be extracted chemically.

In addition to unsaturation and taking on of phosphorous the fatty acids are said by Musser (87) to bear a similar correspondence to the selection of amino acids for body protein in the building of body fat. In this connection Bloor (20) states that with a choice of food the organism builds a depot fat characteristic of its species, but on a diet of selected animal fat the same is stored unchanged in the fat depots of the body. He point out that in poisoning, a mobilization of fat from the depots occurs in the liver where the fat is found to be characteristic of the type found in them. Joslin (59) says that in inanition more fat is deposited in the liver than by fat feeding, and that the former may raise the blood cholesterol by as much as 128% in a few days. He states that all liver fat above 3% is con-

sidered to be that which is composed of fatty acids with a low iodine number which have been mobilized from the fat stores or depots, and is only temporary. He gives 10% fat as the upper limit of this substance in the normal liver which usually contains only 2-3% as does other normal fresh tissue. He points out that the first 3% of liver fat has an iodine number of 135, while depot fat has an iodine number of only 65. He says that liver fat is more highly desaturated than that of muscle or adipose tissue. This seems to agree essentially with Bloor's (20) contention that the liver is the main site of desaturation of the neutral fat, though the latter (20) states that other organs besides the liver have also been shown to contain fat of greater desaturation than the food or depot fat.

Lambie (66) states that the depot fat is in inverse proportion to the liver fat which is in turn inversely proportional to liver glycogen. He points out that the mobilization of fat from the depots occurs through the breaking down of the neutral fat to fatty acids and glycerol which are then resynthesized into neutral fat in the blood by some unknown mechanism. This is essentially what happens in the absorption of food fat from the intestines. Lambie also delegates the liver as the organ

concerned with the desaturation of fatty acids, and further states that this makes them over into more easily oxidizable substances for the tissues. He believes that the liver may also build up the fatty acid molecule into complex phospholipids such as lecithin, which as has been mentioned is a highly suitable form for utilization in building cellular fat. C.H. Best and his coworkers (17, 18, 19) found that in depancreatized dogs receiving insulin the livers of these animals stored much fat having a low iodine number, and that when fed fat this storage in the liver was accelerated. By feeding lecithin instead of food fat they found that the liver did not store fat. This was also true when betaine, a non-toxic oxidation product of the lecithin-toxic dwrivative choline, was administered, and concluded from this that lecithin prevents fat storage in the liver and is essential to intermediary fat metabolism.

Joslin (59) states that it is generally accepted that fat is transported to the liver by lecithin and cephalin in the form of fatty acids where these are desaturated and thus prepared for use in the body. He says that fat in the blood is in three forms: free and combined fatty acids, the former comprising the bulk of neutral fat stored in the body; lecithin, a vehicle for

transportation of fatty acids in the blood stream; and cholesterol, also a vehicle for transportation of fatty acids. Bloor (20) states that the concentration of fat, cholesterol and lecithin in the plasma varies with the species and is undoubtedly influenced by the amount of fat habitually ingested, whereas the corpuscular fat content of all species is approximately the same.

Bloor (20) states that stored fat is found principally in more or less well defined fat depots such as the abdomen, subcutaneous tissue, intermuscular tissue, and around organs. He states that this depot fat is not mormally present in more than small amounts in the active tissues such as the heart, kidney, and muscles, though of course complex lipoid material of the built-in cellular type is found there. Smith and Willius (109) state that the heart normally has fat over its base and atrioventricular groove, around the bases of the great vessels, along the coronaries, interventricular sulci, and right border and anterior surface of the right ventricle. They (108) find that the normal weight of the adult heart averages 294 grams in males and 250 grams in females. They also indicate that the normal ratio of heart weight to Body weight averages 0.43% for males and 0.40% in females, and that the heart weight in either sex may be

calculated from the body weight without error of more than 10%. Joslin, Dublin. and Marks (60) state that,

"The proportion of fatty tissue to total body weight is normally greater in women than in men throughout adult life. Significant differences also exist between persons of the same general build, but differing in musculature."

Grafe (46) states that fat deposits in the body serve three purposes: aid in heat regulation, anchor organs, and protect deep seated vital organs from mechanical injury. Maximow (77) points out that the function of fat tissue is the storing of nutritive material in the form of neutral fat, plus the mechanical function of padding between and supporting organs. He describes adipose tissue as an areolar or loose irregularly arranged connective tissue in which fat cells have crowded out the other elements. He points out that this is the site of the formation of true fat cells which occur singly or in groups especially along blood vessels, each cell consisting of a large drop of neutral fat which reduces the cytoplasm of the fibroblast to a thin membrane in which lies a round flattened nucleus. He adds however, that droplets of neutral fat may occur in any cell of connective tissue, but is not true fat tissue. He be-

lieves that any fibroblast may be transformed into a true fat cell in adulthood as well as in early life, though these cells never undergo mitosis and may lose their fat to be retransformed into a fibroblast. He says that fat enters and leaves the cell in an invisible form, but in inflammation, polyblasts may enter a fat cell and phagocytize its fat and remain within the cavity as densely crowded polyhedral cells. He points out that in those places where fetal connective tissue will later become fat, a rich network of capillaries always develops so that fat tissue contains a good blood supply. Smith and Willius (109) state that a capillary is visible between nearly every two fat cells so that fat is a relatively active vascular organ. Beall (13) states that histologically fat has a good blood supply, each lobule of one-sixteenth of an inch in diameter being supplied by an arteriole which breaks into capillaries drained usually by two veins. He points out that there are at liast three thousand such lobules per cubic inch of fat tissue. Love and Christie (67) in contradiction, state that fat has a relatively poor blood supply, but seem to be in the minority in view of what has been said above.

In spite of the rather uncertain mechanism of

fat transportation and deposition in the body, the manner of the actual oxidation of fat has been more firmly established. Bloor (20) states that the breaking down of fatty acids at the beta position involving two carbon atoms at a time is probable, because most fats have been found to contain fatty acids with an even number of carbon atoms. He says the probability is further increased because fats may be built up from carbohydrate through lactic acid, acetaldehyde, beta hydroxy butyric aldehyde, and finally, by simultaneous oxidation and reduction, to butyric acid. It is also well known that for the complete oxidation of fatty acids to carbon dioxide and water, the oxidation of carbohydrate is essential so that actually as has been said, "the fats burn in the fires of the carbohydrates".

DuBois (36) states that the oxidation of fat alone yields 4.72 Calories for each liter of oxygen consumed, but since fats consume correspondingly large amounts of oxygen (72.5 Molecules of oxygen/molecule of fat which gives off only 51 molecules of carbon dioxide), the respiratory quotient for fat is only 0.707, and much of the oxygen is combined with hydrogen to form water so that for every 806 gm. of tripalmitin, 882 gm. of water are formed. Hence he points out that the body ob-

tains more water from solid fat than from an equal weight of pure water. Wiley and Newburgh (123) state that fat holds water in the body to the extent of 10% of its weight because this much is used when fat is stored and will be liberated when it is katabolized. Grafe (46) with respect to the fluid content of fat itself, cites H. Bozenraad[1] whose figures place the variation between 7-46%, and adds that it can be stated only in general that increasing rates of fatty deposits lead to lowered fluid concentration in them a nd vice versa.

The heat value of one gram of fat according to M. Rubner[2] cited by DuBois (36) is 9.3 Calories, who states that Rubner proved that food oxidized in the body gave off the same amount of heat as if it were burned outside the body, and that all warm blooded animals gave off the same amount of heat per unit of surface. Grafe (46) adds that all the foodstuffs are represented in nutrition in accordance with their caloric value, whether they are derived from the diet or from the substances of the body, a fundamental conception expressed in M. Rubner's

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1. Deutsch. Arch. f. klin. Med., 103:120, 1911.
2. Ztschr. f. Biol., 42: (New Series 24:) 261, 1901.

well known isodynamic law, whom he cites.[1] Grafe says that the different chemical construction of the foodstuffs results in different oxygen requirements for oxidation of each, which is expressed in calories so that measurement of the heat production can readily be deduced from it. He gives 4.6 Calories for protein, 4.686 for fat, and 5.05 for carbohydrate, as the heat value of one liter of oxygen for each of these respectively, and indicates that these values are sufficiently close together that the oxygen calorimetric average per liter inspired may be placed at 4.8 Calories for measuring the basic exchange for all foodstuffs. This means that the respiratory quotient must also be represented as an average figure for measuring the combined metabolism of foodstuffs by oxygen utilization with indirect calorimetry.

Von Noorden (117) points out that the total daily heat production or metabolism consists of three factors: the basal metabolism (960 Cal./sq.m., for adults), energy for work (840 Cal., of which 590 are lost as heat because of the inefficiency of the human organism), and surplus heat production (200 Cal., from the reaction to intake of food due to work of the liver,

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1. Ztschr. Biol., 30:73, 1894.

stomach, and intestines during digestion). Bernhardt (16) states that Rubner later showed von Noorden's surplus heat to be specific dynamic action, and adds that this phenomenon accounts for one-fourth of the total metabolism. Lusk (69) states that Rubner made an allowance of 11.1-14.4% heat loss over and above the starvation minimum for this factor. Grafe (46) allows 2-4% for the specific dynamic action due to fats. Lambie (66) states that fat alone causes a rise of only 2.5% of the caloric value of the food, and Wang and Strouse (120) showed that the specific dynamic action of fat in normal individuals was least of all three foodstuffs. Hence it appears that fat is the most economical of foodstuffs in this respect.

DuBois (36) also states, as does Lambie (66), that the total metabolism or heat production consists of the basal metabolism, bodily activity, and influence of food. The former believes it safe to add from 5-6% of the calories of the food to allow for the total "cost of digestion". He states that in computing the total metabolism an additional 2% should be added to account for small losses of food in the feces which he states are not accounted for in Rubner's factors of 4.1 Cal. for protein and carbohydrate, and 9.3 Cal. for

fat. He states that during muscular exercise the body uses the three foodstuffs in the same proportion when this is moderate, but with increasing severity, carbohydrate is used in greater proportion followed by increasing fat utilization when the former is exhausted. Krogh and Lindhard (65) show that on a carbohydrate diet the R.Q. of normal persons is higher in the basal or post-absorptive state, and prove that in muscular exercise the efficiency with carbohydrate intake is greater than with fat, though both are oxidized. Lambie (66) allows from 1/3 to 1/2 of the basal caloric requirement as sufficient to take care of the energy of activity. Bernhardt (16) however, believes that following work there is a compensatory depression of the basal metabolism even in normal individuals where economy is necessary, so that he would designate post-absorptive metabolism as "standard metabolism". DuBois (36) also indicates that the lowest or basal metabolism is never attained except during profound sleep or prolonged undernutrition, so that the term is really a misnomer with the present method of obtaining the basal metabolism 12-14 hours after the last meal with the subject lying motionless, as is done in nearly all laboratories. Grafe (46) uses the term minimal metabolism which he defines as "the intensity of oxi-

dation, which is a normally well-nourished, healthy individual may not be decreased by any physiological means." DuBois (36) states that measurement of the oxygen consumption is the best way to measure heat production indirectly, but unless the calories are reckoned from the oxygen and R.Q. there may be as much as 2-4% error. He states that expression of the basal metabolism in terms of surface area is most accurately based on the height-weight formula worked out by D. DuBois as follows:

$$\text{Surface Area} = \text{Wt.}^{0.425} \times \text{Ht.}^{0.725} \times 71.84$$

This is not the place for a discussion of the various factors influencing the basal metabolism either in health or disease, but it is hoped that the foregoing enumeration of a few of the facts concerning the determination of the total metabolism will bridge the gap to a discussion of the subject of obesity. In the transition to a consideration of the definition of this disease, it may be mentioned that the normal nutritional requirements of man as pointed out by Grafe (46) are quoted as follows:

"Adult, fasting and at rest---1. Cal./hr./Kg.
Adult, confined to bed without metabolic disturbance---1.2 Cal./hr./Kg.
Adult, with restricted activity
-------1.3-1.5 Cal./hr./Kg."

He also states that the optimum daily fat requirement for humans has not been determined, but concludes from the observations of other workers on rats fed no fats except vitamin A, that for such animals a fat minimum does not exist at all, or at least at a very low level, since they remained perfectly normal. With regard to the manufacture of lipoids within the organism Grafe (46) states that the ability of the body to synthesize cholesterin has been definitely established, but suggests that others may possibly be formed likewise. It has been stated by others that in starvation, when all the fat of the body is used, the animal dies, and that approximately 2gm./Kg./day are necessary to preserve the protein of the body.

THE MEANING AND IMPORTANCE OF OBESITY

Definition and Standards

Obesity comes from the English root obese which is derived from the Latin word obesus meaning "to devour". Dorland (32) has defined it as "an excessive accumulation of fat in the body", and distinguishes between a hyperplasmic type, which consists of an increase in the body protoplasm only, and a hypoplasmic, which is characterized by a decrease in the body protoplasm in addition to an increase in fat. This seems to imply that obesity may be either protoplasmic or adipose in nature so as to include any condition of overweight, but that when fatty in nature is associated with hypoplasia of the body protoplasm. He lists corpulence and fatness as synonyms, but in the present paper adiposity, stoutness, overweight, and overnutrition will also be used synonymously with obesity.

The definition of obesity, the disease, has been made still more confusing by the varied interpretation of the word "excessive", which appears in the definitions of many investigators. Hurry (55) and Lambie(66)

among others, consider obesity as pathological when it interfers with functional activity, the latter stating that "what is excess depends on the point of view". A typical definition as stated by J.H. Means[1] in Cecil's Textbook of Medicine is as follows: "Obesity is a state in which the amount of fat stored in the body is excessive". Other workers have attempted to qualify the word "excessive" by designating the extent or degree of overweight. McLester (81) states that obesity is a condition of the body in which the weight because of excessive storage of fat, is 10% or more above the normal standard weight for age, sex, and height. Other writers designate higher or lower percentages. Joslin, Dublin and Marks (60) say that the definition of obesity is at fault because the standards of normal weight are based on an increase of weight with age, which they add is neither inevitable nor physiologically sound. Similarly, Axtell (7) indicates that increase with age is not normal or physiological, and places the ideal weight of both sexes for age 30 at 135-160 pounds depending on the height.

McLester (80) on the other hand, states that with age a slight increase in weight is physiological.

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1. Phil. and London, W.B. Saunders Co., 1934. (3rd Ed.)

He further indicates (82) that at age 35 a gain of ten pounds, and at age 50 a further gain of ten to twenty pounds is to be expected because of its constant occurrence. He presents a convenient formula derived from life insurance standards which approximately expresses such a physiological gain; normal Wt.(Kg.) = Ht.(cm.) - 100.

Although weight gain in adults is assumed to be normal in standard tables based on insurance statistics , Lambie (66), in support of Joslin and others, does not believe these are the proper criteria from which to judge normal weight. He suggests that the various formulae which have been advanced by others may be more reliable because age is not taken in to account. He cites those of T.R. Harrison[1] as follows:

Males; Normal Wt.(lbs.) = 110 lbs./5 ft. plus 5.5 lbs./additional in. of Ht.

Females; Normal Wt.(lbs.) = 100 lbs./5 ft. plus 5.0 lbs./additional in. of Ht.

Poulton (99) cites from M. Greenwood, E.M. Newbold, and D.I. Cripps another formula, which he states they derived from M. Flack[2], for both sexes as follows:

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1. Failure of the Circulation, p. 115, Baltimore, Williams and Wilkins Co., 1935.
2. Biometrica, 14:316, 1922-23.

Normal Wt. (Kg.) = 0.408 x Ht. (cm.) plus 0.693 x stem length (cm.) plus 70.213.

Lambie (66) suggests that the normal range of variation should be from 15-20% above the average, and prefers to express significant overweight as a ratio of $\frac{\text{Actual Wt.}}{\text{Ideal Wt.}}$. He indicates the normal quotient as 1 to 1.1; up to 1.25 as slight adiposity; 1.25 to 1.50 as medium adiposity; and over 1.5 as marked adiposity. He further states that as a criterion of weight normality, body type or configuration may prove superior to either tables or formulae, as suggested by N. Pende[1], whom he cites. In this connection Dreyer (33) has considered body build of adults up to fifty years without reference to age on the basis of four measurements: height, sitting or stem length, chest girth, and vital capacity; each expressed by simple formulae in terms of the other and tabulated in tables to eliminate calculation for the determination of normal weights of each sex. In the opinion of DuBray (37) this method is superior to other standards, but the 1925 Report of the Committee on Dreyer Measurements in Relation to Life Insurance Underwriting Practice for the Association of Life Insurance Medical Directors (106) revealed

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1. Constitutional Inadequacies, Phil., 1928.

that Dreyer's standards as applied to insurance subjects were inaccurate in differentiating normal from abnormal, and were pointed out as unsafe criteria for judging overweight risks because many of his normals were distinctly abnormal according to insurance standards.

In addition to the weight factor, the great confusion which exists in etiologic classifications of the many types of obesity, only adds to the difficulties of constructing a proper definition of the disease. Obesity has also been considered from a qualitative standpoint, as indicated by Rony (104) who believes that it may exist without overweight because of restricted diet which he desiginates as "masked" obesity and explains as an inherent obese tendency which will become manifest whenever dietary restriction is removed. He also describes a "pseudo"-obesity due to overfeeding and limitation of exercise, which is false only in the sense that if left to follow his own urges, the patient would soon return to normal weight. Kisch (62) describes another kind of pseudo-obesity in patients with an enlarged abdomen, due entirely to a sympatheticotonic inhibition of the movements of the bowels. Poulton (99) has distinguished between the proportion of protoplasm and adipose tissue in considering the severity of the adiposity. Grafe (46) also

leans toward the consideration of a relative type of obesity. He states that all cases of overnutrition cannot be considered as obesity and that it is not synonymous with overweight because it represents a functional disturbance characterized by superfluous fat deposits. He points out that it does not matter whether the surplus weight is great or small and cites C. von Noorden[1] as having reported a type of relative obesity which is not accompanied by striking surplus weight. Aubertin and Coursier (6) consider Wt. – Ht. (metric) as an obesity index.

From the foregoing it may seem that obesity should be defined with an emphasis placed on an increase in the percentage or relative amount of fat in the body, but practically, the total body weight is the only feasible clinical means of determining its presence. For this reason it seems best to use overweight synonymously with obesity. Grafe (46) indicates that although obesity passes as a metabolic disease, it is actually a disease of overnutrition as will be more apparent from the discussion of the etiology in the following chapter.

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1. Die Fettsucht, Vienna and Leipzig, Holder, 1910. (2nd Ed.)

History and Incidence

The history of obesity is so voluminous that space does not permit more than a few passing remarks before discussing the more modern, though perhaps none the more important considerations of the subject. Elsom (39) states that over indulgence in eating dates back to the taking of the forbidden fruit in the Garden of Eden. Riely (103) also says that obesity is one of the commonest and oldest ailments to which human flesh is heir. He adds that Henry VIII became very fat and gouty as did also Charles V of Spain, and that Catherine the Great of Russia had to be carried around in a wheel chair because she was too fat to walk.

William Wadd (118) in his book published in 1816, gave an account of all conspicious fat persons from the earliest period. In addition he stated that Hippocrates, who Adams (1) believes was a contemporary of Socrates and lived the latter part of the fifth century A.C. (460-370 B.C.), spoke of certain inhabitants of the banks of the river Phasis whose bodies were so corpulent that the joints of their limbs were not visible, and cited this as evidence of the antiquity of cases of obesity. He further quoted Hippocrates as saying, "that those who are uncommonly fat die more quickly than the lean". To quote Wadd him-

self, he stated that corpulency "when excessive is not only burdensome, but becomes a disease, disposes to other diseases, and to sudden death". Von Noorden (117) stated that even before the time of Oertel, whose Handbook was printed at Leipzig in 1884[1], the dangers of obesity in heart disorders were clearly recognized, and pointed out that no one stated such dangers so emphatically as he. Von Noorden added that no other writer so forcibly described the great advantages accruing to heart cases so complicated, from therapeutic measures directed toward a reduction of excessive fat, and further indicated that before Oertel's day clinicians thought reduction cures harmful in heart disease because they believed it was weakening to the organism.

Wadd (118) indicated that even Hippocrates laid much stress and wrote largely upon diet, and that Herodicus was the first to apply exercise for the removal of disease and the preservation of health. Wadd himself stated that rigid abstemiousness and constant attention to diet and exercise are required to combat corpulence.

This rather superficial sketch of the earlier

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1. Listed under Obesity in Vol. X of the Index Catalogue of the Library of the Surgeon-General's Office, Washington, D.C., Series 1, 1889.

history of the problems of overnutrition serves to emphasize the persistence of this condition down through the ages. The more recent advances toward an understanding of the problem should be indicated by enumerating some of the outstanding workers of the nineteenth century. McCollum (79) states that Bidder and Schmidt first noted the phenomenon of the specific dynamic action of foods in 1852. Lusk (70) stated that Nathan Zuntz (1847-1920) contributed the first portable apparatus for determining respiratory exchange in man, which was carried to the bedside for the study of disease by Magnus-Levy in 1893. Lusk stated that Max Rubner (1854-1932), the most eminent of Voit's pupils, found in 1883-84, that carbohydrate and fat were interchangeable in nutrition and that 100 Calories of one was the nutritive equivalent of the other, and indicated that this isodynamic law of Rubner was valid except for specific dynamic action.

Other important contributors are listed by Garrison (44) as follows: Carl von Noorden (1895-1911) on dietetics in disorders of metabolism; Graham Lusk (1898-1915) who discovered that specific dynamic action of protein was due to a stimulative effect of certain amino acids; Atwater and Langworthy, on the balance of

nutrition in 1898; R.H. Chittenden, on the minimum nutritive requirement of the body in relation to capacity for work and nitrogenous equilibrium in 1904; F.G. Benedict, on the influence of inanition of metabolism in 1907; and Delafield DuBois, who gave the formula for calculating the surface area in 1915, to which the metabolism of individuals between 20 and 50 years of age is proportional, the normal average basal metabolism for both sexes being 39.7 Cal./sq. meter/hr.

The vast number of contributors in the field of nutrition makes it impossible to mention more than a few at this point, but it is hoped that none of the more important investigators will be omitted in the succeeding pages of this paper. For a more complete review of this phase of the history the reader is referred to "A History of Metabolism" by G. Lusk[1].

Statistics and Significance

In emphasizing the relation which obesity bears to other diseases it is appropriate to begin by quoting von Noorden (117) who stated that,

"Generally speaking, we are more often confront-

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1. Endocrinology and Metabolism (L.F. Barker, Editor), New York, D. Appleton & Co., 1922. (Vol. III)

ed with the necessity of combating obesity for the sake of influencing the course of complicating diseases than of treating obesity for its own sake". Riely (103) adds that obesity in a degree worthy of comment has for some time been appreciated by physicians as a menace to continued health, and always leaves a trail of unfortunate complications. Bulmer (26) states that degenerating disease of a fatal nature in the heart, kidney, and liver are 2 1/4 times more common in the obese than in normals and 3 3/5 commoner than in underweights.

Although insurance tables consider obesity more or less synonymous with overweight, their statistics provide the best evidence there is that the disease not only decreases length of life, but predisposes to the degenerative diseases. The Association of Life Insurance Medical Directors of America (43) in an Interpretation of Some of the Results of the Medico-Actuarial Mortality Investigation, Vol. II, advance proof that there is a heavy mortality among men distinctly overweight whether the abdominal girth is large or not, and that mortality increases with increasing percentage of overweight. Emerson and Manny (40) in a study of the

same report[1], which they state includes males from ages 20-62, find that in the early twenties mortality increases 1%/lb. below average weight for height, while in ages above 35 the mortality increases 1%/lb. above average weight for height.

Dublin and Lotka (34) indicate that although applicants for insurance cannot be taken as representative of the general population, they do furnish in their way a sample of that section of the population comprised within the usual occupationally productive ages. They cite the records of the Metropolitan Life Insurance Company[2] of 60,000 applicants for standard life insurance during 1931, which they state revealed that out of a total of 9% having medical impairments that made them ineligible for acceptance at standard premiums, 2.7% of the total were rejected because of overweight. Heart disease comprised 1.28% and hypertension 0.58%, which were next highest in frequency of those listed.

The Metropolitan Life Insurance Company (85) states that taking the death rate of the normal weight group as 100%, it is noted that overweights as a whole

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1. Report of the Medico-Actuarial Investigation of 1912 for the period 1885-1908. (Vol. II)
2. Medical Impairments and Mortality, 1933.

have a mortality from complicating diseases as follows: diabetes 257%; nephritis 172%; arterial disease 165%; cerebral hemorrhage 157%; heart disease 151%; and cancer 111%. This same company also finds appreciable excesses in death rates among overweights from angina pectoris, influenza, paralysis, appendicitis, cirrhosis of the liver, and typhoid.

Dublin and Marks (35) state that it has long been known that obese are predisposed to the degenerative diseases, and that although at younger ages it is a distinct advantage to weigh a little more than average weight, after 35 years of age persons of normal or less weight outlive their adipose fellows. They state that the examination of the records of the Union Central Life Insurance Company of 192,304 males 20 years of age or over insured from 1887-1908, revealed that body build as represented by weight, when excessive, is a distinct disadvantage which increases with increasing age as well as with increasing weight. They suggest that the extra body bulk taxes the vital organs, putting a burden of work particularly on the heart, the kidneys, and the blood vessels.

From this evidence it is apparent that obesity is deserving of careful consideration by all who expect to practice medicine.

ETIOLOGY AND ITS FACTORS

Classification

It is obvious that unless some satisfactory clinical classification of types of obesity can be adopted, a division of the various kinds encountered depends on a clear understanding of their causes. Grafe (46) states that except for a small percentage of typical sharply defined forms, the outward manifestations or localization of the adiposity cannot be used to define the origin of the disease. Since a clinical classification may not correspond to an etiological division, the difficulties of ascertaining the origin of obesity are apparent. Although a knowledge of the genesis would appear to be of utmost importance in the treatment of this disease, there are many including Campbell (27), Dunlop and Lyon (38), Wilson (125), and others, who believe that any case of obesity regardless of type will respond to dietary treatment alone. On the other hand, McLester (81) states that certain types, especially the endocrine, do not respond to diet and Riely (103) considers that the exogenous obese have a uniform distribution of fat, whereas the en-

dogenous do not and thus seems to favor a clinical consideration of classification. This would seem to dispel the necessity for an etiological classification of the disease, and Gurney (48) suggests that the clinical classification is less confusing than the etiological, although he adds that both are difficult. Barr (11) on the other hand, states that the distribution of the fat no longer furnishes a sure means of classifying endocrine obesities clinically because the same girdle type of distribution is found in either pituitary or hypothalamic lesions.

Lambie (66) states that the physician is called upon to treat obesity as a disfigurement, as a disease, and as a symptom of other diseases, while Master and Oppenheimer (76) consider that obesity should no longer be regarded as a symptom, but rather as a disease.

It is interesting to note the simple classification of Dearborn (31) who says that "some are born fat, some achieve fatness, and some have fatness thrust upon them", and that of Ebstein, cited by McLester (81), who divides obesity clinically into "those who inspire envy, those who occasion laughter, and those calling forth sympathy".

It is apparent from what has been said concern-

ing the definition of the disease that the weight is the essential factor in determining the presence of obesity clinically, and no attempt is made in the following etiological discussion to indicate the amount or severity of the condition encountered in the various types. A qualitative as well as a relative type of obesity has already been discussed, which exists as a sort of "occult" obesity and which would be rarely recognized clinically unless symptoms referable to an abnormal percentage of fat in the body suggested it. In addition McLester (82) divided obesity into a plethoric and an anemic type of obesity, the former seen in ruddy complexioned males of hearty demeanor having high red blood cell counts and hemoglobin, whereas the latter occurs mainly in females of sedentary habits and pasty complexion with an anemic blood picture. Although it may be concluded that the distribution of the fat may not furnish the correct criterion of its origin, from what has been said above, its characteristics may prove useful if only as a hint to the clinician. And since it is obviously not feasible to attempt an arbitrary classification, the writer will undertake only a discussion of the pathogenesis of the various types which have appeared in the literature.

Exogenous versus Endogenous

In commencing a consideration of the causes of obesity it is important to emphasize that regardless of its exact genesis, this disease is always the result of a positive energy balance. Grafe (46) indicates that obesity is always due to overfeeding, where overfeeding stands for an excess of nutritional calories above the amount actually required. He adds, however, that overfeeding does not always produce obesity, but that when it is evident that this is the most important factor concerned, such cases may be labeled as exogenous. Most authors including DuBray (37) and Gauss (45), describe exogenous obesity as that resulting from excessive intake or decreased output or both, and stress the purely environmental nature of this type. McLester (81) designates this as an alimentary or indolence type, but also suggests an hereditary or familial tendency of this group toward good appetite, digestion, and phlegmatic temperament. Lambie (66) designates the exogenous group as nutritional or acquired, leaving out heredity as a factor. DuBois (36) on the other hand, states that the exogenous obesity is not strictly exogenous because greediness and laziness are certainly inherent bodily traits. He adds that neither is the use of the word "simple" adequate to

describe exogenous obesity, as this type is often difficult to cure. Newburgh and his coworkers (89,90) however, consider that obesity is always caused by an over abundant inflow of energy which arises from either human weakness including over indulgence and ignorance, or conditions which cause lessened activity or a lowering of the basal metabolic rate. They believe that there is no specific metabolic abnormality in obesity and therefore all cases are "simple" in the sense that they result from either excessive intake or decreased output. They also seem therefore to include an hereditary factor in exogenous obesity.

Silver and Bauer (107) on the other hand, outline the insufficiences of the "balance" theory of obesity which , they state, presupposes a primary increase in appetite or primary decrease in energy output, and stress the congenital or hereditary nature of the obese state as of prime etiologic importance. Dublin and Marks (35) stress that weight is a component of two forces: congenital or hereditary skeletal structure which is fixed at maturity and determines the weight, and peculiarity in the dietary and habits of the individual which are subject to control; and are of the opinion that by far the more important factor is that of inherited body structure. Wil-

son (125) states that whether obesity is to be explained on the basis of energy intake alone or energy intake plus endocrine gland disturbances, is not entirely settled, but indicates that the preponderance of evidence points toward the latter. Rony (104) points out that human obesity is basically endogenous, but that a disturbance in the internal fat regulating mechanism may be aggravated by exogenous factors, and that heredity may set the level of sensitivity for such a regulatory center. In spite of the many interpretations concerning the basic cause of obesity which have been indicated by the foregoing, it seems sensible to consider that obesity is never purely exogenous or entirely endogenous in nature, but it is permissable to use the former term to designate those cases in which environmental influences predominate.

Exogenous

Under the exogenous type of obesity, appetite and exercise are the principal considerations. DuBois (36) considers that the former is governed by the muscular activity of the preceding twenty-four hours. He also states that the extra food taken in excess of the requirement of the depleted store-houses of the body produces a rise in metabolism because of its specific dy-

namic action so that the excess is burned, but if well nourished the individual becomes more energetic so that stored excess fat will also be burned. He adds that when the appetite does not meet the demands the stored fat will be called upon also, and when the intake remains insufficient the specific dynamic action will be reduced and a gradual lowering of the basal metabolism will result from the undernutrition. He believes further that this sub-caloric intake may stimulate the appetite so that a fairly constant level of fat storage is maintained, this habitual level possibly governing the eating habits of the individual. McLester (80) also believes in some sort of a regulatory apparatus which keeps normal persons at a fixed weight, despite excesses in the diet or the exercise, the desire for either of which being kept at a balance. Grafe (46) regards the gauge of this fine adjustment as the appetite and the feeling of satiety although he adds that the mechanism of this control is by no means clear. He cites E. Neisser and H. Braeuning[1] who present the idea that persons with large abdomens have less of a feeling of satiety due to the fact that the feeling of fulness which is

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1. Munchen. med. Wchnschr., p.1955, 1911.

caused by intragastric pressure, does not make itself felt as soon or as strongly as in normal individuals. Harrop (50) states that the sensation of satisfaction of fulness is dependent on satiety of the food which property depends on its fat content and therefore regards a milk and banana diet as an ideal reduction regime. He recommends 6 large bananas, 1000 cc. of skimmed milk divided into 3 meals daily with a fluid intake of 6 large glasses of water which he believes does not interfere with nitrogen balance for two weeks. McLester (80) indicates that carbohydrate also has a high satiety value, a fair amount of which, Harrop says, is also present in banana.

Booth and Strang (21) advance evidence to indicate that satiety depends on an increased temperature of the skin which they find is lower in obese than in normals after ingestion of food. Grafe (46) points out that some regard the mechanism as a central nervous influence from the effect of either impulses from the digestive organs, or a lowered concentration of foodstuffs in the blood upon certain brain centers. DuBois (36) states that it is not necessary to assume an interference of the ductless glands in the weight regulating mechanism of average individuals involving familiar pro-

cesses. Others regard that there are definite inborn tendencies which govern the appetite, whereas some regard habit as the important factor in satiety. The question arises as to why some individuals on the same intake and exposed to the same environmental factors become obese, while others do not.

Constitutional

Strouse and Dye (112) conclude from their own observations as well as from cases reported by German writers, that certain types of obese maintain weight on a diet below the normal intake required to maintain a caloric balance. McLester (80) presumes this so-called constitutional obesity of Strouse to result from an error in metabolism, the consideration of which will be discussed.

Basal Metabolism

In regard to the basal metabolism in obesity Strouse and his coworkers (113) in a review of the earlier literature, also point out that obesity uncomplicated by endocrine disorder, which had previously been shown to have a variance in the basal metabolism by various workers, is erroneous when recalculated from the DuBois scale of computing body surface. They conclude from an examination of 61 subjects that neither excess under-

weight or overweight is associated with a constant change in basal metabolism, and that obesity can not be caused by changes in it. Means (84) concludes from calorimetric measurement of oxygen that the majority of obese subjects however extreme, show no alteration in the basal metabolism expressed in terms of surface area, and that in cases where occasional slight reduction occurs there is also clinical evidence of disturbed internal secretion. Preble (100) also observes that the basal metabolic rate is within normal limits in 1000 cases of obesity, which were 10 or more pounds overweight.

Bernhardt (16) on the contrary, advances evidence to show that, although 66% of 100 mixed cases of obesity had basal metabolic rates within normal limits and showed the same or greater increase in metabolism during work as normals, those who gain weight on a basic caloric intake are found to have a basal metabolism below that obtained in the morning, especially following muscular work or during sleep. He finds that these "negative phases" are of varying length and degree, but are sufficient to indicate that the usual morning basal metabolic rate obtained does not represent the whole day's metabolism.

Rony (104) however, points out that the basal metabolism is an unimportant factor in obesity since in comparison to normals, obese subjects have a greater surface area and hence a greater basal metabolic rate. He suggests the use of a Basal Metabolic Ratio, expressed as a per cent deviation from the normal basal metabolism of an individual with average normal weight of the same age, sex, and height. He states that this Ratio averages a 30% increase per 100 pounds body weight in obese subjects, whereas the ratio is low or minus in lean persons. He adds that the reason obese persons have a relatively higher Ratio is because of the preponderance of inactive tissue or fat imposed on the basic tissues, plus the increased work of the heart and respiratory muscles, plus lowering of the "luxus consumption" from prolonged overfeeding and exceptionally, plus hyperthyroidism. He uses this high ratio in obese cases to contracict Bernhard's "negative phase" in which he states the cases exhibiting this phenomenon had abnormally high basal metabolic rates and also points out that some of the series had no negative phase.

Grafe (46) however, criticizes Rony' findings of frequent rises in the basal metabolism of obese, and reports that in his own series all cases showing a rise

were complicated by other diseases and doubts if it can ever occur in uncomplicated obesity. He adds that even though occasional decreased metabolic rates (only 2.7% in his series) occur in obesity, the basal metabolism cannot be used to solve the problem of endogenous obesity since this lowering occurs in other diseases.

Lambie (66) suggests that although the basal metabolic rate is normal in obesity, this may actually mean an increase with respect to the active tissues since most of the body bulk or fat is inert tissue. It is also suggested by Axtell (7) that although the surface area in obesity is greater than in corresponding normal weights, it is less in proportion to the total body weight than in lean persons. This fact would suggest that the greater the obesity, the lower becomes the basal metabolism in proportion to the amount of bulk necessary to diminish. Also the point that the active tissues have an increased metabolism in obesity, suggests the opposite necessity of increasing the body bulk to enlarge the surface area and so increase the energy output to favor destruction of the inactive tissue or fat. It may at least be concluded that the so-called basal metabolism is usually not changed in uncomplicated obesity.

Metabolic Influence of Food

Another consideration in the energy "balance" theory of obesity is that of the influence of food upon metabolism. Since the discovery of the phenomenon of specific dynamic action, many theories have been advanced to explain it, but that of G. Lusk (68) which regards it as the result of amino-acid stimulation of the body cells, is as good as any. Grafe (46) regards M. Rubner's[1] theory of nitrogen retention as fallacious, but states that Rubner and others early showed the effect of both specific dynamic action, and a secondary effect designated as surplus heat formation by Rubner and luxury consumption by others, resulting from overnutrition with proteins. Lusk (69) has termed luxury consumption the secondary dynamic effect. Grafe (46) is the chief exponent of this theory of "Luxus Konsumption" and he and his coworkers have shown that the specific dynamic effect is actually increased by overfeeding with carbohydrate as well, so that this phenomenon he adds, may be used to explain why some people do not gain weight in the face of overnutrition with a variety of foodstuffs. He explains it on the basis of superimposed daily oxidative increases,

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1. Gesetze des Energieverbrauchs, Vienna, Deuticke, 1902.

and regards it as an adaptation to overnutrition the same as occurs in the opposite direction with fasting or undernutrition. Grafe states that he and E. Eckstein[1] have found that luxus consumption does not occur in an animal after thyroidectomy and suggests from this evidence that the thyroid acts as a compensatory gland which not only prevents obesity when functioning normally, but may explain the basis for lack of obesity in all cases of gonadectomy, an observation made by Bernhardt (16). Grafe (46) suggests that this conception of a compensatory activity of the thyroid forms the bridge to an understanding of endocrine obesity wherein failure of the glands of internal secretion permits obesity to develop without increased intake because of lowered or absent luxus consumption. Wiley and Newburgh (124) advance evidence to cast a doubt upon the theory of "Luxus Konsumption". From the study of a very thin subject in whom the basal metabolism and total transformation of energy was recorded while on a maintainance diet of 3000 calories and a hypernutritive diet of 5000 calories, they find that the overfeeding results in an increment in the metabolism which can be entirely

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1. Ztschr. f. phys. Chem., 109:125, 1919.

accounted for by specific dynamic action alone after deducting that produced by the increase in body surface resulting from the increase in weight. Grafe (46) however, criticizes their results because the specific dynamic effect was not measured, and because the subject gained weight, indicates the probability that the case was one of those who did not have the capacity to react to increased food intake by an increase in oxidation, many of which he states he has observed.

In regard to specific dynamic action in obesity, Wang and Strouse (120), from a study of obese, normal and thin individuals fed separate protein, carbohydrate, and fat meals, find that the obese react less to all three foodstuffs than either thin or normal subjects, and observe that the greatest depression occurs following protein. Bernhardt (16) and Grafe (46) both observe a lowered specific dynamic action in obesity, the former believing however, that its effect on the total metabolism is not sufficient to account for the condition and finds it entirely absent in hypogonadism, while the latter considers it a possible cause, especially in the constitutional type where he finds it to occur more frequently than in the purely exogenous form, and suggests that Lauter's few contradictory cases were complicated

by other disease. DuBois (36) states that a great many obese patients studied in America have shown nothing unusual in their specific dynamic action. It appears that neither lowering of the basal metabolism, nor either lowered primary or secondary specific dynamic action of food may be used to explain many cases of so-called constitutional obesity.

Muscular Activity and Metabolism

In regard to muscular activity it has been mentioned that Bernhardt (16) could find no decrease in the metabolism in obese compared with normals during muscular activity, but did suggest a compensatory after-effect designated as the "negative phase" which might indicate a greater economy of energy in obesity. DuBois (36) however, cites studies of Wang, Strouse, Smith, and Morton[1] and states that they were unable to demonstrate any evidence of a "negative phase", and furthermore that rather their results indicate a decreased efficiency in obese subjects during work. This conflicts with the studies of Gessler,[2] cited by both Du Bois and Grafe (46), in which the latter states he found

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1. Wang, Strouse and Morton, Arch. Int. Med., 45:727, 1930; Wang, Strouse and Smith, Arch. Int. Med., 45:1004, 1930; Ibid, 46:40, 1930.
2. Deutsch. Arch. f. klin. Med., 157:36, 1927.

less energy expended by obese during work than in normal weight subjects of the same age and height. DuBois (36) is of the opinion that the present evidence points to a decrease of efficiency in obese subjects, but admits that an abnormal lowering of the metabolism in the obese during sleep is possible.

Newburgh and his coworkers (89, 91, 93) have taken a forward step in the problem of determining the influence of activity on the total daily metabolism, by measuring the insensible loss of weight from which computation of the total metabolism is possible. They (93) indicate that the insensible loss of weight is equal to the insensible water or perspiration, plus the carbon dioxide expired minus the oxygen inspired, which represents approximately 24% of the total heat production, and more recently (91), probably nearer 25%. They state that the water vapor accounts for the greater part or all of the insensible weight loss and that for every gram of the former lost, 1.58 Cal. is removed. The insensible water loss is measured by correcting for changes in the body weight from the following formula: Loss of Wt. = (initial body Wt. plus ingesta)– (final body Wt. plus urine plus stool). They derive the carbon dioxide and oxygen values from the known dietary constituents(93).

They indicate the convenience of using such a measure of the metabolism with which the activity of the patient need not be restricted, but at the present time they have not directly applied it to muscular activity influence in obesity.

Anomalous Metabolism

Other workers attempt to explain obesity on the basis of a peculiarity in the handling of the products ingested for metabolism. Hagedorn, Holten, and Johansen (49) believe that obesity is due to a disturbance in the regulation of the combustive processes in the organism, analogous to the anomaly occuring in diabetes mellitus. They think that, since Krogh and Lindhard find a high respiratory quotient in post-absorptive normals on a carbohydrate diet, obese patients might show a low respiratory quotient in the post-absorptive state because of rapid transformation of carbohydrate to fat. Their results on 30 obese fed a high carbohydrate diet lead them to conclude that the mean R.Q. in obese is lower than in normals, indicating an abnormally increased transformation of carbohydrate to fat. This is essentially what Wang and Strouse (121) find when obese, normal, and thin subjects are fed large meals of each of the three foodstuffs. They conclude that obese subjects derive less

energy from fat than either normal or thin subjects soon after meals, which explains their tendency to fat storage because mainly carbohydrate is being metabolized for storage as fat at that time.

In connection with studies of the respiratory quotient used to determine the partition of foodstuffs in obesity, Krantz and Means (63, 64) find that epinephrine as a metabolic stimulent produces a definitely lower rise in the R.Q. of obese as compared with normals, and conclude that obese individuals have less glycogen and more fat available for metabolism, the most readily available foodstuff being oxidized under such circumstances, which they add, is fat in the case of obese subjects. Lyon, Dunlop, and Stewart (71) in a series of 34 observations of the respiratory quotient of obese subjects fed on sub-caloric diets with reduced carbohydrate, find evidence to conclude that in the undernourished obese subjects, fat is converted to carbohydrate, but add that under normal conditions the normal metabolism does not necessarily take place in this way, a fact previously noted from the work of Stewart, Gaddie, and Dunlop, in the chapter concerning normal fat. DuBois (36) states that the findings of Lyon and his coworkers (71) are difficult to account for if Lusk's modification of the

old Zuntz and Schumburg table is correct, since they observe a decrease in the R.Q. after an addition of carbohydrate.

McClelland, Spencer, Falk, and DuBois (78) find a higher threshold of ketosis in an obese subject as compared to normals, all being fed on a relatively high ketogenic diet, and assume from this that obese have greater efficiency in the utilization of fat. Hetenyi (52) finds a marked drop in the blood fat level to below normal in undernourished obese subjects which also showed a decreased alimentary hyperlipemia. He interprets these results to mean that mobilization of fat from the fat depots is impaired, while these same depots have a markedly increased ability to store circulating fat in obesity. He suggests that it may be a "depot" disease though admits this is not the final solution. Rony and Levey (105) find that the average fatty acid content of the blood is somewhat higher in the obese, but after the administration of one pint of 20% cream observe that this level is either decreased or increased.

From the foregoing it should be evident that, since the R.Q. is greatest with oxidation of carbohydrate and least with fat, protein occupying an intermediate position, interpretation of this quotient with

regard to the principal foodstuff being oxidized is extremely misleading, since it represents the sum total of oxidative processes in the organism as measured from the respiratory intake and output. As Krogh and Lindhard (65) suggest, it is quite possible that fat may be deposited in one part of the body while it is being mobilized for combustion from another, which would indicate that little definite knowledge regarding the intermediary interconversion of foodstuffs is to be obtained from studies of the R.Q. alone. The ketogenic studies have the same defect since the threshold of the appearance of ketone bodies in the urine is usually designated by an R.Q. of below 0.76. Hence, although there is some evidence to indicate that a few obese individuals may have some metabolic anomaly to explain their tendency to excessively store and economize the burning of fat, it is too controversial to be conclusive. Bernhardt (16) suggests using the R.Q. as a prognostic sign. He states that a low R.Q. gives good prognosis whereas if high, a bad prognosis is indicated.

Water Balance

In attempting to explain the failure of certain of the cases of obesity to lose weight on a subcaloric intake, Newburgh and his coworkers (90, 92, 123)

are opposed to the conception of a metabolic disturbance in obesity and explain the discrepancies between the expected weight loss and the actual loss or gain on the basis of water retention. They compute the actual expected loss of body tissue by comparing the total energy and nitrogen output with the energy value of the diet. They determine the water balance by considering all the excretory water (urine, stool, and insensible perspiration) against the ingested liquids, water in the food, water of oxidation, and preformed water. They determine the insensible water loss as was shown above (93). The water of oxidation is determined from the composition of the metabolic mixture ingested, and the preformed water from the amount required in storage, ie., the amount left behind when tissue is katabolized. Newburgh (89) states their results completely account for an absence of weight loss in underfed subjects because of the instability of the water content of the body, and adds that this explodes the main support for the hypothesis that obesity is caused by internal disease. He and Lashmet (92) conclude that gain or retention of weight on a restricted caloric intake means water retention and applies to normal as well as obese persons.

Bartels and Blum (12) however, from a study of obese, normals, and underweights subjected to Volhard dilution tests, concluded that underweights had more marked water retention than the non-dieting obese subjects and the latter had a more sustained urinary output than normals and did not retain fluids well. This does not conflict with Newburgh's findings, but simply contributes the idea that normals show more retention than the obese who are not on a diet. They suggest that since the latter do not retain fluids well, it might be better to force fluids in obesity for psychogenic reasons. In addition to the storage water required, which amounts to an extent of 10% of its weight in the case of fat as pointed out previously by Newburgh, Grafe (46) states that fat tissue absorbs water like a sponge, which he adds is not to be confused with edema, and emphasizes the importance of considering this fact in judging total body weight. He does not state whether or not water retention can explain all cases of constitutional obesity as Newburgh contends. Campbell (27) points out that depot protein is a colloid capable of retaining water in varying amounts according to the amount of accompanying salts and the acid-base balance so advises a moderate restriction of protein in reduction diets.

It has been indicated that the basal metabolism, metabolic reaction to food, energy economy, and a metabolic anomaly cannot be used to explain certain cases of so-called constitutional obesity. DuBois (36) says "we must conclude that constitutional obesity is accompanied by no abnormality of metabolism striking enough to be demonstrated by our present methods" and adds that it seems to be in many cases an hereditary disease.

Endogenous

Before considering the hereditary factor, it might properly be argued that constitutional obesity also belongs with this group in as much as internal metabolic derangement has been considered in the preceding discussion. As was pointed out at the beginning of this chapter, the separation of all etiologic factors into two separate groups is impossible, so that much that appears in the foregoing as well as what follows may have certain characteristics which suggest a different interpretation of their classification.

Heredity

It has already been intimated that we cannot disregard the operation of an hereditary factor in any of the various types of obesity. Although the general

concept that obese persons are of a phlegmatic disposition is prevalent, Dunlop and Lyon (38), in a study of 523 cases of obesity find that only 10.4% were of phlegmatic temperament, whereas 59.7% were of an excitable disposition. They also find that 69.2% of the cases gave an hereditary history of overweight fathers or mothers. They find only 8.2% of the cases with an endocrine (endogenous) disturbance, whereas purely dietetic cases amount to 37.2%. The remaining 53.6% of cases were mixed, with both exogenous and endogenous factors present. Of the entire group it is significant that 45% were excessive carbohydrate eaters which has been frequently pointed out as a factor in obesity. In as much as excessive carbohydrate intake has been considered as a factor in many cases of exogenous obesity, it is pertinent to mention at this point that Ogilivie (94) has pointed out that it is difficult to tell whether the hyperinsulinism which increases hunger, or the dietary habit which increases the demand for more insulin is primary.

To return to the hereditary aspect of etiology, the Metropolitan Life Insurance Company (86) indicates from a study of the parents of 294 overweight employees that 50% of them were overweight, and in 25% both parents

were overweight. Gurney (48) points out from the work of C.B. Davenport[1] that body build follows the laws of Mendelian inheritance in which there are three gametic factors, one corresponding to dystrophy of the thyroid, one to dystrophy of the pituitary, and one which may be a metabolic factor affecting the actual metabolism of the cells themselves. He believes this hereditary factor may explain why the onset of obesity is manifest in one among many exposed to the same environment. From his personal study of 75 females, 15 or more pounds overweight, he concludes that pregnancy or a major operation is the most common factor associated with the onset of obesity in 63 of the patients, and that the incidence of parental obesity is much greater in obese than in non-stout women. He also finds segregation present after a study of the progeny of different parents and states that Davenport considers this evidence for Mendelian inheritance. Preble (100) finds his group of 1000 cases of obesity comprising the ages between 30-60 consists predominately of females, and suggests that this may be explained on the basis of ante and post-partum feeding by

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1. Body-Build and Its Inheritance, Washington, D.C., Carnegie Institution of Washington, 1923.

obstetricians.

Silver and Bauer (107) believe in the importance of a primary peripheral tissue "lipophilia", a theory propounded by G. von Bergmann[1] cited by Grafe (46), who states that this theory is that of a lipomatous tendency in which condition there is abnormally facilitated fat production and impeded fat destruction. Grafe also mentions the theory of I. Lichtwitz[2] which pictures a weakness of fat cells due to an increased separation between lipolytic ferment and fat in the cells, and that of W. Falta[3] who believes primary hyperinsulinism causes obesity because with an overload of sugar in these patients, the sugar curve fell below the initial level after it had reached its peak. Grafe (46) states that such a drop in the sugar level is not present in all obese cases, and Tyner (116), in a study of 1000 individuals half of whom were normal and half obese pre-diabetics 5% or more above normal weight, all fasted and given a Brill test meal, finds that the obese group have sugar levels above

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1. Die Fettsucht, Oppenheimer's Handb. d. Biochemie, 7:562, 1927. (2nd Ed.)
2. Stoffwechselkrankheiten, Fortbildungsvortrage Diesbaden (v. Herxheimer), p. 205, Berlin, Karger, 1926.
3. Wein. klin. Wchnschr., 1928, p. 905; 1930, No. 10

the fasting level two hours after the meal. Rony and Levy (105) find that the amount of sugar tolerance in obese subjects varies directly with the degree of fat tolerance, which suggests that either might be a measure of insulin function. Grafe (46) admits that a functionally active pancreas might be a factor in the development of obesity. He suggests that the principle of a lipophilia in the peripheral tissues may explain the peculiar distribution of fat observed in the endocrine disorders.

Endocrine versus Neurogenic

In regard to the endocrine origin of obesity much has been written, and DuBois (36) points out that it is conceivable that an endocrine disturbance so slight as to produce only common obesity may exist without the usual marked stigmata of endocrinopathy. Grafe (46) also considers an endocrine mechanism in connection with his theory of "luxus konsumption", as has been pointed out. Others are inclined to place emphasis on a regulative center in the central nervous system. Bernhardt (16) states that in the etiology of obesity, the endocrines do not play the first role, but adds that the decisive factor is the function of a hypothalamic regulative center lying somewhat behind the tuber cinereum

in close proximity to the pituitary where the connecting link is not clear, but might explain how the hypofunctioning ductless glands may alter its ability to regulate the weight. He compares it to the temperature center and believes that peripheral tissue changes such as behavior, hunger, and thirst may also influence it. He finds that lumbar puncture with fluid removal lowers the basal metabolic rate in obesity. In connection with peripheral influences upon such a center, Rony (104) considers the fat content of the body as determining the level for the threshold of its activity as has been mentioned. He also emphasizes that exogenous factors may aggravate the center.

A step toward the definite proof of the existance of such a center has been taken by Smith (110) who has experimentally produced a syndrome of adiposity, genital atrophy, and increase in the total body length of rats by artificial injury to the tuber cinereum in the hypothalamic region of the brain. He states that this syndrome differs from that following hypophysectomy in that no atrophy of the thyroid or suprarenal cortex occurs and the genital atrophy is much less profound. This emphasizes the point made previously that not all obesities exhibiting peculiar distribution of fat can be

classified as endocrine.

Also the frequency of obesity following encephalitis lethargica where there is inflammation involving the hypothalmus suggests the importance of the central nervous system in the maintainance of normal body weight. Gauss (45) regards the post-encephalitic obesity as the only strictly true type of the endogenous class and Hunter (54) regards organic lesion of the hypothalamic region as the principal factor in endogenous obesity in contradistinction to the absence of any organic lesion characterizing the exogenous form. The close proximity of the hypothalmus and the pituitary makes the distinction between pure endocrine and neurogenic obesity very difficult.

It has long been appreciated that hypopituitarism produces a girdle type of obesity resulting from compression of the active elements of the gland principally by chromophobe adenomata or craniopharyngiomas. It is also fairly well established that the chromophile tumors produce hyperpituitarism, acromegaly resulting from those composed of eosinophil or alpha cells, and a peculiar type of "buffalo" obesity described by Cushing (28) resulting from hyperactivity of the basophil or beta cells. He describes this form as having plethoric facies with fat only on the face, neck, and trunk associ-

ated with exaggerated secondary sexual characteristics and frequently large red striae on the abdomen and thighs which are occasionally painful. He explains the occasional tendency to hypertension in these patients by an hypothesis (29) that the basophil cells from the anterior lobe of the pituitary invade the posterior lobe, the extracts of which are known to produce a constant moderate elevation in blood pressure. Walters, Wilder, and Kepler (119) observe a similar syndrome in adreno-cortical tumors which further complicates the exact endocrine origin of this condition. Also, Cushing (28) frequently observes a concomitant glycosuria.

Thompson and Cushing (115) are able to produce a similar adiposity in animals injected with a pituitary gonad-stimulating hormone. To explain the accompaniment of glycosuria in this endocrine syndrome, Barr (11) has referred to the work of B.A. Houssay[1] and B.O. Barnes[2] who he states found that the pituitary inhibits the effect of insulin because hypophysectomy in depancreatized dogs lessened glycosuria and hyperglycemia. He also concludes

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1. Houssay and A. Biassotti, The Hypophysis, Carbohydrate Metabolism and Diabetes, Endocrinology, 15:511, Nov.-Dec. 1931.

2. Barnes and J.F. Regan, The Relation of the Anterior Pituitary to Carbohydrate Metabolism, Endocrinology, 17:522, Sept.-Oct. 1933.

that this pancreatic-inhibiting hormone can act only through the suprarenal glands, because C.N.H. Long[1] has found that in depancreatized cats, adrenalectomy also lessens glycosuria, but is fatal unless cortical extract is given by which life is prolonged and fatal ketosis to pituitary extract does not occur, as in dogs. These reports suggest how either a pituitary or adreno-cortical tumor may produce glycosuria by depressing the insulin function of the pancreas, and further emphasizes the inter-relationships of all the endocrine glands. Barr (11) describes an adreno-cortical syndrome of hypercorticoadrenalism, produced by cortical suprarenal tumors, as a combination of hirsutism, amenorrhea, and obesity, plus a constant moderate elevation in blood pressure, which differs from Cushing's Basophilism in some respects.

Lambie (66) points out further the vast connections which exist with respect to the nervous system, because he states that water retention may be due to starvation, involvement of the neurohypophyseal mechanism (reverse of diabetes insipidus), or lack of thyroid se-

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1. Long and F.D.W. Lukens, Observations on Adrenalectomized Depancreatized Cats, Science, 79:569, June 1934; Observations upon Hypophysectomized Depancreatized Cats, Proc. Soc. Esper. Biol. and Med., 32: 326, Nov. 1934; Observations on a Dog Maintained for Five Weeks Without Adrenals or Pancreas, ibid., 32:392, Nov. 1934.

cretion. He states that other workers have actually found nerve tracts supposedly connecting the so-called hypothalamic weight-regulating center with lower brain centers and possibly the hypophysis. G.M. Griffiths (47) in describing the Laurence-Biedl Syndrome of adiposity, polydactyly, retinitis pigmentosa and mental retardation, states that we cannot separate the pituitary or diencephalic centers in this condition, which he indicates Biedl believed was a primary cerebral adiposity resulting from a congenital malformation with hydrocephalus and pressure on the diencephalic metabolic centers, because pituitary signs are also seen.

Maddox (74) and Wilson (125) both, in describing Dercum's original syndrome of adiposis dolorosa, associated with asthenia or depression and paraesthesia in addition to painful indurations in the subcutaneous layer of the trunk and limbs, occurring in women around the menopause, point out that the condition is not a clinical entity because all cases do not show consistent endocrine glandular changes. The former states that both generalized and localized painful tumor types of this condition occur, and adds that Waldorp postulates a derangement of the diencephalic centers controlling fat metabolism in this condition also. Gauss (45) indicates that Dercum's

disease and Lipomatosis are not true obesity, so may be out of place in this discussion although they serve to indicate the importance of some relationship of the nervous system to fatness. Babonneix and Denoyelle (8) state that the pituitary is not responsible for obesity accompanying essential hydrocephalus where the causal lesion is in the walls of the third ventricle, and use these facts to refute Cushing's theory.

From the foregoing some explanation for the observation of Czerny (30) that obese children are known to have higher fever with infectious disease than undernourished, may be postulated from the proximity of the heat and weight centers both of which are assumed to be located in the hypothalamus. Grafe (46) and others suggest that the disturbance in temperature control in the obese is on the basis of decreased radiation from a compromise of skin function which might contribute to the promotion of the obesity also. Another metabolic factor in the promotion of obesity not previously mentioned, is indicated by Dearborn (31) who suggests that the condition may be due to unusual smallness of the lungs which thus minimizes the destruction of fat.

In concluding this chapter it may be added that the relationship of obesity to hypogonadism occurr-

ing in either eunichoidism or the menopause is not thoroughly understood and Grafe (46) believes that only exceptionally is this disorder accompanied by decreased metabolism. In both myxedema and cretinism of hypothyroidal origin, the basal metabolism is lowered, but this finding is not constant in hypopituitary obesity. In the case of the hypocortico-adrenal activity occurring in Addison's disease the basal metabolism is lowered, but as undernutrition is also a cause of decreased oxidation, its presence in this disease may account for the existence of this finding. It should be emphasized that the endocrine types of obesity in which stigmata of endocrinopathy are definite, comprise but a small proportion of the obese patients. Preble (100) says the ductless glands are rarely an etiologic factor. Silver and Bauer (107) state that endocrine obesity occurs in only 3% of the cases studied.

In the next chapter but little attention will be focused on the complications of endocrine obesity, since in these types obesity occurs as a symptom rather than a disease.

THE PATHOLOGY IN COMPLICATING DISEASES

Uncomplicated Changes and Symptomatology

The morbid effects of obesity are dependent to a large extent on the duration and severity of the condition. Grafe (46) states "it must be apparent that the presence of great fat accumulation cannot help affecting the function of the organs in the long run". J.H. Means[1] in Cecil's Text-Book of Medicine points out that,

"In the milder grades of obesity there is simply an excess of fat in the normal fat depots, such as the subcutaneous and retroperitoneal tissues, the breasts, and the omentum. In the severer grades, fat infiltration is found also in parenchymatous organs such as the heart and liver."

Axtell (7) indicates that obesity is a danger signal which not only aggravates the cause of its genesis, but produces further deranged function and real path-

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1. Phil. and London, W.B. Saunders Co., 1934. (3rd Ed.)

ology. He adds, "obesity itself is a potent cause of further obesity, aggravating itself, increasing its own causes and multiplying its ill-effects". It appears therefore, that unless obesity is of a sufficient degree to affect more than the usual sites of fat deposition, there is little or no real anatomical pathology present. The metabolic changes concomitant with obesity have already been discussed in connection with its causes, but as these may also predispose to certain other diseases, further reference to them will be made later.

The present chapter is concerned with the effects of obesity as a disease rather than a symptom, and therefore need not include the symptomatology of the neural or endocrine types in which the pathology is predominately the result of hormonal or nervous disturbance. Only the effects of excessive weight or fatty change then, is the ultimate aim of the present consideration. What are these morbid changes which confront the majority of obese patients as they present themselves to the physician?

MacCallum (72) states that in obesity fat collects in the subcutaneous and intramuscular tissues, bone marrow, mesentery, omentum, retroperitoneal tiss-

ues and epicardium, kidney, and the orbit. In very fat persons it penetrates the heart wall and appears underneath the endocardium. Master and Oppenheimer (76) state that obesity is a disease of slow onset tending in the long run to shortness of breath, weakness, and a decreased duration of life. They say that symptoms arise simulating myocardial failure, the most common being dyspnea, fatigue, palpitation, dizziness, and headache, but add that these five main symptoms are all relieved by dietary reduction of weight and therefore assume them to be characteristic of uncomplicated obesity. Axtell (7) states that fat in the panniculus is always accompanied by fat in the internal organs. Buck (25) says that fat deposits occur most frequently around the heart, omentum, abdominal wall, and arms and legs.

Before undertaking a discussion of the various complicating conditions associated with obesity, a few general concepts of the nature of fatty changes as they occur in the internal organs will be pointed out. In regard to the distinction between the terms of fatty infiltration and fatty degeneration, Reid(102) points out that the term fatty degeneration is a misnomer because it does not result from the breaking

down of the protein of the cells, but on the contrary is really an infiltration of fat in the form of circulating lipoids into the cell, as a result of increased permeability from cell injury, or the result of chemical change of the invisible congugate lipoid content of the cell such that it becomes visible microscopically by assuming a colloidal form. Smith and Willius (109) cite the work of G. Rosenfeld[1] and G. Herxheimer[2] who both agree that fatty change in the cytoplasm is really an infiltrative process so that both fatty degeneration and infiltration are similar in the sense that both occur as a result of deposition of fat from external sources.

Although these statements indicate that fatty degeneration should not be interpreted to mean a transformation of cellular protoplasm into fat, it is still acceptable to differentiate the terms on the basis of intra and extra or intercellular for fatty degeneration and infiltration respectively, in spite of the fact that the source of the fat appearing in the cells of any of the organs so affected is usually extracellular.

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1. Uber die Herzverfettung des Menschen, Zentralbl. f. inn. Med., 22:145, Feb. 9, 1901.
2. Uber Fettfarbstoffe, Deutsche med. Wchnschr., 27:607, 1901.

That such changes appear in conditions other than obesity is well known. The workers cited by Smith and Willius above, state that the microscopic appearance of globules of fat in otherwise normal tissue cells appears as a result of a disturbance of cellular nutrition plus toxemia. It is obvious therefore, that this change does not characterize the organs of an obese person since no toxemia is present unless superimposed upon it. Maximow (77) has pointed out that neutral or stored fat may occur in any cell of connective tissue so it is apparent that when excessive fat is stored in the body it may occupy almost any intercellular location in addition to its normal existence as true adipose tissue in the fibroblasts of areolar tissue. Hence in obesity the change is that of an excessive distribution of depot or neutral fat which as has been indicated previously, is normally found in only small amounts in the active tissues such as the heart, kidney, and muscles (Bloor, 20). From this author it has also been noted that although the mechanism of the disappearance of fat from the blood is uncertain, it is known to accumulate in the liver, bone marrow, spleen, and muscles in the order named. Also his statement of the evidence that the source of ex-

cessive fat accumulations comes from either ingested or depot fat because of similarity of iodine number of their fatty acids, would suggest that other organs show fat deposition only after the depots have been completely filled. Fatty liver is usually considered as either infiltrative or degenerative though as in the case of the heart, the fat comes from other parts of the body. However, in obesity the fat is present without much cell degeneration whereas in poisoning or acute yellow atrophy degeneration is more pronounced than infiltration.

So much then, for general pathological considerations. In the following paragraphs a discussion of the various complicating conditions commonly associated with obesity will be attempted.

Complications or Sequelae

Cardio-Vascular

Cardiopathy Hurry (55) discusses the vicious circles encountered in obesity, and commences by pointing out that cardio-vascular disorders are the most important associated conditions of obesity. He indicates that the corpulence imposes an extra load on the myocardium because of the loss of proportion between the size of the heart and the total body weight, additional

capillaries to supply the extra fat tissue, and because of a resulting increase in the volume of blood. As a result of this extra load the heart hypertrophies and sooner or later decompensates. He points out that the heart itself becomes infiltrated with fat and may undergo fatty degeneration. Beall (13) regards fat as a parasite and stresses the fact that its presence requires extra work of all the vital organs. He computes that each pound of fat contains 4,600 ft. of blood vessels so that an obese person 30 lbs. overweight would have an extra 25 mi. of blood vessels for which the heart must do extra work to propel the blood for the nourishment of this extra tissue. He also indicates that the heart decompensates easily.

Axtell (7) suggests a pseudo-hypertrophy of the heart due to fat and believes that it is crippled further not only by an increased quantity of blood, but also from the upward push of the diaphragm which causes a transverse placement with loss of the apex impulse. Barker (9) presents a case of obesity with dilatation of the heart and signs of decompensation and states that the obesity explains the cardiopathy because of presumable masses of fat in the epicardium and pericardium, heightening of diaphragm by fat in

the abdomen, and the 80 pounds extra weight. More concerning the diaphragm will be mentioned later.

McLester (80) also points out that the fatty changes of the myocardium make the heart less able to meet even the demands of a normal body weight. Buck (25) indicates that fat deposites around the heart restrict the pericardial space besides producing increased weight and degeneration of the organ. Preble (100) in his study of 1000 cases of persons 10 lbs. or more overweight finds that 662 show some evidence of cardiac impairment. DuBray (37) notes three common cardiovascular conditions associated with obesity, namely, coronary sclerosis, hypertension, and atrophy of the heart muscle.

From the opinions of the above observers it would seem that cardiac impairment in obesity is principally on a mechanical basis. Brown and Keith (23) however, in a study of the total circulating volume of the blood and plasma in 14 cases of obesity by the dye method, find that after reduction by diet, excercises, and thyroid medication, either a decrease or an increase in the total circulating blood volume occurs and if the former, evidence of anemia is present. Reid (102) on the other hand, indicates that although clinically the

the obese state is detrimental to the heart, it is not satisfactory to explain it on the basis of increased work. He believes that the dietary of those who become obese is deficient in vitamins and minerals, especially calcium, which he indicates is necessary for proper cardiac function as has been shown experimentally, and suggests this as a better explanation of heart dysfunction in obesity. Mac-Dowell (73) even concludes from an analytical review of the literature, that cardiac disturbance in the obese is due more to an endocrine upset, which he feels is responsible for the obesity in the first place. Most workers, however, seem to favor a mechanical explanation as the cause of heart impairment in obesity.

Smith and Willius (109) in a post-mortem study of 136 obese all 13% or more overweight, compare the size of the heart to the body weight and conclude that obese people have a higher average cardiac weight, but in those exceptions where the heart is smaller in proportion to the total weight, this disproportion is a factor in circulatory inadequacy in addition to the usual impairment in cardiac activity and nutrition produced by the infiltrated fat. They indicate that even large hearts, independent of asso-

ciated pathologic changes may occasionally fail or even result in death. These workers (108) note from the cases studied that all died from a variety of conditions and, although all showed varying increases in subepicardial fat (without intracellular fat in the muscle cells) sufficient to increase the burden of the heart, conclude that obesity producing cardiac failure consists in most instances of adding a burden to that imposed by some disease already present such as hypertension or coronary sclerosis. Maranon and Bonilla (75) report a case of sudden death from fatty degeneration of the heart in a female age 29 who weighed 157 Kg. and was 1.6 M. in height. Interestingly enough the history of the case revealed that the woman had been thin until age 18, when after contracting syphilis, commenced increasing in weight a few months later.

Master and Oppenheimer (76) have made a very impressive study of the exact circulatory situation in uncomplicated obesity by observations of the blood pressure, pulse, X-ray and electrocardiogram. Their X-ray findings reveal a sthenic habitus, elevation of the diaphragm, and an enlarged widened heart with a hypertrophied left ventricle and hazy left border ob-

scured by apical pericardial fat. The electrocardiograms show obese patients to have sinus arrhythmia, left ventricular preponderance, and inversion of the P and T waves in lead III. They find that 67% of the cases show hypertension in proportion to the severity and duration of the obesity. The pulse is commonly accelerated and circulatory exercise tolerance is lowered. They are able to relieve all the above findings after reduction of weight, and conclude that this fact amply explains the improvement frequently observed in valvular heart disease, hypertension, and coronary disease after weight reduction. Faber (41) reports a case of arrhythmia with signs of cardiac weakness in a patient weighing 146 Kg. which was relieved permanently by Carell dietary and reduction after quinidin.

Proger (101) also finds a left axis deviation and flattening or inversion of the P wave and inversion of the T wave in lead III only, in the electrocardiograms of a large percentage of uncomplicated obese persons, but states that with ventricular hypertrophy the left axis deviation is usually associated with an erect T wave in lead III. This would indicate that the left axis deviation alone is not diagnostic of left ventricular hypertrophy in obesity, unless

associated with an erect T wave in lead III in which case its presence would be suspicious. The inverted T wave might also suggest coronary disease though this condition usually also shows a disturbance in the preceding S-T segment.

Grafe (46) points out that the increased demands made upon the heart and vessels often lead to early sclerosis in obesity, especially of the coronary vessels. He adds that there is also a tendency to thrombosis and formation of emboli and that differential diagnosis between angina pectoris and fatty heart is difficult since a high diaphragm may produce a definite aortalgia. Aschoff (4) suggests that an excess of fatty substances in the blood plasma has been shown to favor the development of atherosclerosis because of the formation of calcium phosphate from cholesterin esters with which the tissues are asphyxiated. Reid(102) believes that the arteriosclerosis may be used to explain some of the heart impairment encountered in obesity. Hurry (55) has indicated that angina pectoris may complicate obesity because of the irritability of the overloaded heart and points out that both arteriosclerosis and chronic interstitial nephritis are frequent complications of obesity.

In all of these associated conditions it is difficult to determine which factor is primary. Angina pectoris is frequently associated etiologically with arteriosclerosis, obesity, gout, and nephritis, whereas coronary occlusion or thrombosis is considered to result from hypertension and arteriosclerosis and frequently is preceded by angina. It is also generally accepted that fatty degeneration of the heart muscle is frequently the associated pathologic change observed in chronic myocardial degeneration or fibrosis (interstitial myocarditis) which is usually the result of essential hypertension or chronic interstitial nephritis associated with hypertension. Fatty degeneration also occurs in chronic valvular disease as well as in prolonged infection, chronic poisoning, and severe anemia, but is rarely found in uncomplicated obesity, which on the other hand is characterized by a fatty heart which Smith and Willius (109) prefer to designate as "adiposity" of the heart. They use this term to designate fatty infiltration which has been pointed out as one of the principal mechanical factors interfering with normal heart function in obesity.

Arteriosclerosis Since arteriosclerosis is usually considered a result rather than a cause of hy-

pertension, it is difficult to explain the mechanism of primary sclerotic changes in obesity on a purely metabolic basis. Riely (103) states that hypertension is a compensation for increased peripheral resistance especially in those with fixed-calibre sclerotic vessels and indicates that since an abnormality of the cholesterol metabolism occurs in obesity, it is probable that these people have a tendency to arteriosclerosis from atheromatous deposits. Dublin and Marks(35) point out that the causal factors in arteriosclerosis, organic heart disease, nephritis and cerebral hemorrhage have much in common and often suggest the effect of body weight on the elasticity of the blood vessels. They add that Aschoff's theory regarding the relation between tissue fat and arteriosclerosis certainly fits the case of overweights, at least with respect to premature death from degenerative conditions. Joslin(58) points out that there is a difference in location of the degenerative vascular process, being in the extremities with diabetes, and in the coronaries, cerebral or renal arteries in the obese.

Axtell (7) believes that arteriosclerosis and obesity have a common etiology, but points out that obesity contributes to the former by causing

toxic blood products from imperfect metabolism. He points out that the obese first have hypotension due to a weakened heart and later a pre-sclerotic hypertension from the toxemia. He says these factors predispose to apoplexy as well as chronic nephritis, excessive fat deposits and portel stasis also contributing to the latter. It is well known that chronic interstitial nephritis is merely one of the manifestations of a cardiovascular-renal hypertension syndrome. Preble's (100) study of 1000 cases of obesity reveals that 463 with or without a diagnosis of chronic nephritis, show albuminuria as evidence of some kidney impairment. Von Noorden (117) considered obesity a complication rather than a cause of atrophic nephritis (contracted kidney) and indicated that in all associated conditions obesity should be regarded as the complication, since its treatment improves the prognosis in the associated pathology. Grafe (46) also does not regard obesity as the primary predisposing factor in contracted kidneys though admits that they are encountered fairly often in the disease. He states that in uncomplicated obesity, albumin and hyaline casts in the urine are not uncommon.

Although the several observers mentioned a-

bove seem inclined to relate the arteriosclerosis in obesity to an increase in the cholesterol content of the blood from prolonged excess food indulgence, Bruger and Poindexter (24) state that the findings of most workers in this connection are controversial. They point out that in essential hypertension, diabetes mellitus and arteriosclerosis an increased cholesterol has frequently been observed, and that their relation to obesity has been stressed for many years, the latter supposedly being a causative factor in these degenerative diseases. In a study of 94 obese subjects 20% or more overweight, they find that in 53 of the exogenous type uncomplicated by other disease, the plasma cholesterol is within normal limits. In 25 complicated by the metabolic disorders of essential hypertension, arteriosclerosis and diabetes mellitus the plasma cholesterol is augmented. In 11 with arthritic complications the infectious arthritics show a normal plasma cholesterol, whereas the hypertrophic types have significant elevation of the plasma cholesterol. In the remaining 11 obese with causative endocrinopathy the hypothyroids and acromegalic show an increased cholesterol of the blood, while the hypoovarian subjects have values within normal limits. They conclude

that a high caloric intake is not accompanied by a rise of the plasma cholesterol in humans, but when present in obesity complicated by degenerative disease is to be considered a result rather than an etiologic factor in these complications. These observers used Sackett's modification of the Bloor method for determination of the blood cholesterol. Musser (87) more recently also indicates that obese develop degenerative disease before there is an elevation of the blood cholesterol. As will be pointed out later the supposed increase in the cholesterol of the blood of obese patients has also been used to explain the frequency of cholelithiasis in obesity.

Hypertension It has already been pointed out that, in spite of the fact that arteriosclerosis is usually considered a result rather than a cause of hypertension, Axtell (7) and Riely (103) have both implied a sclerosis not preceded by hypertension in obesity. It is certainly true that a sclerosis of the arterial system would require a compensatory increase in the blood pressure to overcome the resulting increased peripheral resistance. It is accepted that arteriosclerosis due to old age or intoxication or infection can precede hypertension, but in these types

the intima rather than the media undergoes proliferative changes so that a gradual obstruction rather than an actual reduction in calibre of the arteries results. Hence, it is only where the calibre is reduced by spasm that hypertension is primary, the later sclerosis resulting from a degeneration of an over-fatigued media of the vessels subjected to prolonged increased tension. It is therefore conceivable that obesity might produce a primary sclerosis on a toxemic metabolic basis, except for the fact that uncomplicated obesity shows no hypercholesteremia from which an atherosclerosis might develop according to Ashoff and others. Foster (42) states that "one can find no adequate evidence for the belief that hypertension is a predominant factor in the causation of arteriosclerosis" and further that "even though some types of nephritis may possibly be of vascular origin, their genesis cannot be traced through arteriosclerosis to hypertension". These statements favor the possibility of arteriosclerosis in obesity without hypertension.

In addition to the work of Master and Oppenheimer, other observers frequently find a hypertension in obesity without arteriosclerosis, which responds to dietetic reduction in weight. Terry (114) indicates

that most fat females seeking medical attention have hypertension which exists without findings suggestive of nephritis, diabetes, and syphilis, He states that in all cases on a high protein-low calory diet there is a lowering of weight, together with a lowering of blood pressure.

Preble (100) finds the blood pressure above normal in 1000 cases of complicated obesity in all age groups over 20, which showed an average drop of 18/10 after a ten pound reduction in weight. Buck(25) also finds the blood pressure up in all obese without cardiac dilatation, which is lowered by reduction unless associated with dilatation of the heart in which case the accompanying low blood pressure is increased. Hartman and Ghrist (51) from a study of the records of 2,042 patients normal or otherwise 15 years or more of age of both sexes conclude that weight must be a dominate factor in determining systolic blood pressure, but find no logical relation of the diastolic pressure to body weight. The Metropolitan Life Insurance Company (86) finds after a course in weight reduction for 294 of its overweight employees, that of 33 who had mostly hypertension or heart disease with hypertension, 17 were better clinically after 5 years and uniformly

showed an appreciable fall in blood pressure. Of the 294, 81% lost an average of 15 pounds at the end of the course, while at the end of one year of 224 available, only 32% had continued to lose weight by voluntary dieting. After 5 years only 21% of 193 available showed further loss of weight, so the Company concludes that continued medical guidance is necessary, if excellent results obtained during treatment are to be maintained, because self discipline is too severe for most overweight patients who are generally inclined toward self indulgence.

It might appear from the above that hypertension could be considered to be a symptom of, rather than a complication or sequela of obesity. Aubertin and Coursier (6) in studies of the blood pressure in 94 obese persons with the same obesity index (Wt.—Ht. metric) indicate that sedentary life, excessive carbohydrate intake and mild drinking habits favor obesity and hypertension, but point out that only in those predisposed to these conditions is this true, since others under identical conditions develop neither obesity nor hypertension. They reject completely the assumption that obesity is a cause of hypertension and suggest that their frequent coincidence has led to the association

of apoplexy and obesity whereas the high blood pressure is really the apoplectic factor. Aubertin (5) adds that although he found frequent hypertension in stout persons, it should be regarded as a complication rather than a sequela. Pedrazzini (97) believes that accumulation of fat disturbs the normal elastic play of the spinal dura which makes possible the entrance of blood into the tissue-packed skull, so urges respiratory abdominal massage in obese and all persons of the apoplectic type to facilitate venous flow in the spinal plexuses.

It is generally accepted that obesity may be a factor in essential hypertension, but the fact that the latter occurs also in persons of spare build does not suggest the former as a true cause. Symptomatic (non-essential) hypertension occurs in cerebral lesions, nephritis, toxemias of pregnancy and hyperthyroidism and if the hypertension which has been shown to exist in obesity is of this type, the only other possible connection besides arteriosclerosis (already considered) is through the cerebral or endocrine obesities. Barr(11) points out that hypermedullary-adrenalism from suprarenal medullary tumors with excessive epinephrine, is associated with paroxysmal high elevations in blood pres-

sure and at death is characterized by kidney and vascular changes similar to those seen in essential hypertension. His description of a constant moderate elevation in blood pressure with an adreno-cortical tumor syndrome mentioned previously, suggests another endocrine factor in the cause of essential hypertension.

It has already been mentioned that Cushing (29) postulates an invasion of the posterior lobe of the pituitary by basophile cells of the anterior lobe as a basis for hypertensive states, one of which occurs in his so-called "buffalo" type of obesity. He also indicates that the number of basophilic cells is known to increase with age and are more numerous in hypersthenic individuals. In as much as the role of the endocrines and central nervous system in obesity is so imperfectly understood, it can only be surmised that the latter may indirectly bear an etiologic relation to hypertension through them. It is possible that obesity and hyperpiesia may have a common origin though at present it seems better to consider high blood pressure in obesity as symptomatic on the basis of a compensation to overcome the need of excess tissue for nourishment.

Riely (103) states that the pressor substances involved in hypertension in the obese is unknown, but

points out that guanidin, which is an end product of protein, is such a substance, so that protein over-feeding such as might be present in obesity, may predispose. He adds that carbohydrate over-feeding does not produce hypertension except in the otherwise predisposed. DuBray (37) states that obesity as a factor in hypertension is mainly mechanical and that there is no clinical evidence to confirm an etiological connection between obesity and high blood pressure. The fact remains, however, that the two are commonly associated and that treatment of the obesity relieves the hypertension.

Metabolic

It has been indicated previously that the degenerative diseases of arteriosclerosis, essential hypertension, and diabetes mellitus have been considered metabolically related to obesity for many years, and that the mechanism of this relationship is somewhat controversial. This controversy is the principal reason why arteriosclerosis and hypertension are considered above rather than under this discussion.

Diabetes In connection with diabetes another viewpoint of the role of hypertension is indicated by Beck, Fowler, Koenig and Bowen (14). These workers

made an X-ray study of 96 obese patients who were divided into diabetics, borderline, and normals according to their glucose tolerance, to determine the presence of calcification of the arteries of the lower extremities. They find no evidence of calcification of these arteries in elderly early diabetics or in obese prediabetics. Further study reveals no evidence to show that hypertension or retinal sclerosis can be correlated with the obese patient's ability to use glucose, the incidence of hypertension being about the same in non-diabetic obese as in the diabetic obese. They add however, that it is their belief that hypertension is essentially related to obesity, rather than diabetes. They conclude that obesity increases the liklihood of both diabetes and hypertension whereas the latter is not a certain contributing factor in diabetes. Musser and Wright (88) however, in studies of sugar tolerance tests on a group of 30 hypertensive obese females without glucosuria, find a lowered sugar tolerance, which does not occur in another group of non-hypertensive obese patients given the same amount of dextrose, so conclude that obesity, hypertension and hyperglycemia comprise a definite syndrome. They add that no single factor accounts for the trisyndrome

but that each contributes to a vicious circle which ultimately leads to a well marked vascular sclerosis. They believe obesity to be the most important factor, because in these patients a lowered sugar tolerance is present and reduction in weight often lowers the blood pressure and produces a rise in the sugar tolerance to normal. These results seem to point to obesity as the principal factor in the hypertension of diabetes, but do not corroborate the conclusion made by Beck and his coworkers above, who stated that hypertension was not a contributing factor in diabetes. Whether or not hypertension in obesity increases the severity of the diabetes or the sclerosis or both, it can at least be stated that all are intimately related in some manner.

In considering the effect of obesity on the insulinogenic function of the pancreas it has already been suggested under the discussion of the etiology that increased food intake may be either a factor in or a result of pathologic changes observed in this organ. Ogilvie (94) states that he made an autopsy study of the percentage area of islet tissue in each pancreas of 19 ordinary fat persons with mainly a subcutaneous and mesenteric distribution, which was com-

pared with that observed in 19 control lean subjects, all 38 subjects being sugar free and having died only as the result of unrelated pathology. Each pancreas was sectioned from the head, body, and tail and stained by the Azan method, 15 microscopic fields of each section being projected on note book paper from which tracing and weighing of the areas could be done for purposes of calculation. He finds that 68% of the pancreas of the obese subjects possessed islands whose average area was definitly greater than normal, although the number of islands was not increased. He adds that only one case showed an island with well marked central fibrosis suggestive of transition to the diabetic state. He indicates, however, that islet hypertrophy does not necessarily imply an increased activity and that normal islets are observed in a large percentage of diabetics. He suggests that excessive carbohydrate eating which is often present in obesity, may produce an islet hypertrophy and lead to a hyperinsulinism with increased hunger, to set up a vicious circle, but that whether the hypertrophy is the cause or effect is difficult to determine.

It does seem to be true that obese persons show some evidence of exhaustion of the isles of Lang-

erhans whether from overeating or other cause, as shown by numerous glucose tolerance tests. John (56) has performed glucose-tolerance tests on 12 cases of obesity and finds that five show evidence of diabetes. He indicates that diabetes or the pancreas should be considered in all obese persons. Of Preble's (100) 1000 cases of obesity, 700 had glycosuria. Axtell (7) points out that both diabetes and obesity have a depressed glycogenic function and the obesity aggravates or further depresses glycogenesis, so that digestive glycosuria develops, which later terminates in frank diabetes. He also indicates that depressed glycogenic function leads to a greater appetite which furthers the obesity. He adds that the glycogenic depression in obesity is accounted for by the fact that the liver is the first organ to deposit fat which impairs its glycogen storage ability. He also attributes diabetes in obesity to fatty changes in the pancreas, the latter of which he believes always occurs. Beeler and Fitz (15) from results of alimentary glucose tolerance tests on their series of non-diabetic obese patients at 10 pounds over normal weight for age, sex, and height, compared with similar control tests on thin non-diabetics and mild diabetics, conclude that some o-

bese have normal glucose tolerance curves and excrete only small volumes of urine and sugar because of some metabolic disturbance probably an endocrinopathy, whereas other obese have a high sugar curve and excrete abnormally large quantities of glucose in a voluminous urine. They indicate that the first group is not likely to develop diabetes whereas the second group may develop the disease.

It has been indicated previously by Rony and Levy (105) that tolerance to fat and sugar in obesity bears a direct relationship. Joslin (59) states that all obese have lowered carbohydrate tolerance whether they ingest fat or carbohydrate previous to the test, and indicates that in obesity the strain on the pancreas from overeating is a greater factor in producing diabetes than the quantity or deposits of fat itself. He adds that rapid increases in weight are more harmful to the pancreas than gradual increases because there is not time for a compensatory hypertrophy. Joslin believes that lack of carbohydrate in the diet causes fat deposition in the liver because clinically, yellow atrophy is improved by feeding carbohydrate. He wonders if the over-insulin production induced by overindulgence in food favors the transformation of carbohy-

drate to fat which is deposited in the depots, while the liver fat is depleted because of the accompanying increased glycogenesis. As Joslin has pointed out, carbohydrate fed along with fat reduces the liver fat, but on fat alone the liver fat is increased as was pointed out from Best and his coworkers (17,18,19) previously. The latter also find that lecithin, like carbohydrate, when fed with fat, produces reduction in liver fat. Lecithin alone, with insulin in depancreatized dogs also produces a prolongation of life with a glycosuria, which is absent when fat is given instead, and the animals eventually die with fatty livers. Joslin (59) adds that evidently fat feeding with insulin alone in these animals produces no glucogenesis in the liver since there is no glycosuria at the death of the dog. He asks the question as to where sugar in the urine comes from when depancreatized dogs receiving insulin are fed lecithin and fat only, since more is recovered than is possible from the glycogen and protein metabolism. Apparently it might come from the lecithin which has also been shown to be essential in the intermediary metabolism of fats. Lusk (69) states it does not come from the fatty acids.

From the above facts it would seem that insu-

lin is an excellent fattening substance, but that when the pancreas is unable to compensate for the demands of excessive intake, the obese person becomes diabetic and loses weight. In addition his liver becomes fatty because of the depression of glycogenic function and there is a decrease of the depot fat. Weber (122) describes a "lipogenic diabetes" depending on or induced by obesity or a tendency to obesity. He believes the fact that dietetic treatment cures obese mild diabetics, is proof of obesity as a cause of diabetes. He points out, however, that in grave diabetes obesity may not occur because of lack of cell metabolism, insulin causing a latent obesity to appear. Beall (13) sums up the problem in the following sentence, "If a diabetic can gain weight he is lucky, but if he does, he is unlucky".

It is interesting in passing to point out that von Noorden (117) believed obesity to be a protection against diabetes and that diabetics did not tolerate reduction cures well.

Rony (104) also believes in the exhaustion of the islets of Langerhans on the basis of excessive intake. John (57) has also indicated his agreement with this belief and, in a study of 528 cases of diabetes in an attempt to discover if obesity plays an important

role in development of the disease, finds that nearly all are or have been overweight regardless of sex and that the percentage of overweight is high compared with data on the weight of non-diabetics from the Equitable Life Assurance Society of New York. Anders and Jameson (3) in a series of 1306 cases of adiposity (including diabetes in 119) note that the incidence is higher in females than in males in the age group above 40, which they point out is an explanation of the greater incidence of diabetes in the former after 40. They add that obesity is the most potent single predisposing factor in diabetes. Adams (2) from the height and weight records of 673 cases of diabetics admitted to the Mayo Clinic, finds that 91% are overweight (82.9% over 10% overweight) before their diabetes begins. He states that no sex differences are noted, and adds that obesity is also probably an important factor in the development of diabetes in the young since over 30% of cases under 20 years were over 10% overweight. He also finds that over half of 1000 cases of obese diabetics have preventable obesity ie., that due to faulty living habits.

Joslin (59) indicates that obese diabetics are not so common as formerly because the proportion of

young diabetics is increasing whereas the proportion of older diabetics is decreasing, and obesity occurs more after age 35 than before. He differs with Adams, because he points out that children illustrate that obesity is not a universal causal factor since they are more rarely overweight. He believes that heredity is little by little displacing obesity as a cause of diabetes, so that now we need only to combat obesity in the hereditarily disposed diabetic. Tyner (116) has made studies to prove Joslin's statements. He determined the carbohydrate tolerance curves in 500 each of normals and prediabetics 5% or more overweight before and 2 hours after a Brill test meat, and concludes that prediabetes occurs about equally in obese and normals or underweight, and that this condition is correlated rather with age, the peak of its incidence being reached in the seventh decade. From a study of their hereditary and familial history he finds, however, that obesity with direct (parental) diabetic heredity shows an increased incidence of prediabetes, whereas thinness or obesity with only familial heredity does not.

Joslin, Dublin, and Marks (60) have made a study of 4596 adult diabetics 5% or more above average weight which were seen by Joslin from 1898-1928. They

find that at the time of maximum weight 78.5% were males while 83.3% were females, and of 3094 cases at the time of onset of diabetes 62.7% were males and 67.4% were females. Only 7.9% men and 6.3% women had always been 5% or less underweight, and less than 1% of the whole group had always been 20% or more underweight. They conclude that the chief constitutional factor in the onset of diabetes is overweight. They add, however, that next to overweight, heredity is the most important of the other significant etiological factors in diabetes and state, "Indeed, the factors of obesity and heredity are probably closely linked." These workers indicate that the obese who become diabetic have for the most part inherited susceptability, while obesity acts as the immediate exciting factor and is the most common factor in the etiology of diabetes. They suggest that,

"It is possible and even likely, that the connection between adiposity and diabetes is not a causal one and that both reflect some underlying imbalance in the functioning of the body, probably of endocrine origin."

From the foregoing evidence it seems best to consider obesity in association with heredity as a cause of dia-

betes mellitus.

Gout It is generally accepted that overeating, especially of protein bears a direct etiologic relationship to gout, and that gouty subjects are often overweight. It might be supposed therefore, that gout and obesity are the result of a common causal factor, rather than that one predisposes to the other. The literature is very meager concerning obesity as a factor in gout. Von Noorden (117) pointed out that gout (arthritis urica) was frequently found with obesity, but indicated that with the latter, prognosis was better than in the thin persons where great articular destruction is comparatively common. He added that obese gouty subjects were easier to put on a regime of diet and excercise because of their obesity.

Axtell (7) indicates that impairment of secretory function of the liver might result in gout, among other functional disorders. Grafe (46) states that the relations between obesity and gout are obscure, probably because of lack of knowledge of the latter disease. He indicates that gout is more often associated with the exogenous than the endogenous form of obesity. He suggests that the close relation of obesity and gout to diabetes indicates a common central nervous origin

since the centers in the fore-brain which regulate the sugar, uric acid and fat balance are close together. Apparently the relation of obesity to gout is merely that of an accompanying condition, both resulting from a common etiologic factor.

Digestive

Cholelithiasis Complications of the digestive system are frequently seen in obesity. In addition to bulimia, dyspepsia, constipation, etc., Hurry (55) mentions that obese subjects are prone to develop liver and gall-bladder disease. Axtell (7) points out that fat deposition in the liver so decreases its secretory function that a resultant acholia is responsible for occasional white stools, alternating constipation and diarrhea, urobilinuria and cholemia. He indicates that some damage to hepatic cells from fat infiltration may even rarely favor cirrhosis of the liver whereas a flabby abdomen, impeded diaphragm and sedentary habits produce mechanical stagnation in the gall bladder. He states that one in every 2 or 3 women who are fat develop gall stones. The relation of the saying "fair, fat, and forty" to gall bladder disease is well known. Stasis is also recognized as one of the etiologic factors in diseases of the gall bladder, and cholelithiasis is believed to be favored by impairment in function of the

liver cells to secrete bile salts which render cholesterol soluble in bile and prevent its precipitation. Stasis also favors higher concentration of bile which also favors precipitation of cholesterol, especially if the cholesterol content of the blood is high as pointed out by Musser (87). As mentioned previously, he points out that the liver cells do not excrete cholesterol esters, but only cholesterol, so that the ratio of these two compounds in the blood may be more important than the total plasma cholesterol.

In connection with arteriosclerosis, evidence of high plasma cholesterol in obesity was shown to be controversial. Joslin (59) however, insists that high fat diets or overnutrition causes a high blood cholesterol. He indicates that complications of high blood cholesterol include diabetic coma, xanthoma diabeticorum, cataracts and arteriosclerosis, the latter two of which he states are not proven, but are suggestive in some cases. Love and Christie (67) also believe that the obese show a higher blood cholesterol which favors the tendency to gall stone formation which they add is favored by the lethargy. It has also been indicated that some evidence exists for the opinion that high blood cholesterol follows rather than precedes degenerative

disease. This might suggest the latter as the factor in hypercholesteremia rather than obesity. The fact remains, however, that high blood cholesterol favors gall stones, and that obesity whether or not responsible for the high blood fat is associated with them. Perhaps obesity acts only as a static factor.

Dunlop and Lyon (38) in their series of 523 cases of obesity find that 5.5% have been operated for gall stones and, although constipation is found in 40.9%, it is of no greater incidence than in non-obese. Bulmer (26) states that chronic cholecystitis and gall stones are much more frequent in the obese.

Heyd (53) indicates that cholelithiasis is frequently concomitant with obesity in females and parallels a metabolic defect of obesity as the result of basic dysfunctions and altered metabolism. He states that during the course of surgical operations he is impressed with the frequency in which the liver is grossly proportionally smaller in obese than the stature and age of the patient would suggest to be normal. He believes there is a distinct tendency for the liver to be inversely proportional to the added weight over the normal body weight, and that this fact may obviate that the liver does not possess all of the protective adaptations inher-

ent in normal liver function. Axtell (7), it has already been indicated, states that portal stasis as well as fat infiltration favors damage to the liver and that the resulting hepatism and cholemia favor hematogenous infection of the gall bladder.

Pancreatitis Among the other digestive complications pancreatitis has frequently been indicated as commonly associated with obesity. Axtell (7) points out that the obese have a fatty pancreas which not only favors diabetes, but also fragile vessels so that they are easily ruptured, resulting in colic, vomiting, and pancreatitis. Love and Christie (67) point out that acute pancreatitis occurs most frequently in obese, but add that the reason for this association is obscure. Heyd (53) states that pancreatitis in the obese occurs predominately in males where it is associated with pathological conditions, which in some inexplicable manner parallel the obesity. He also finds duodenal ulcer associated with obesity in males on the same basis. A possible explanation for the role of obesity in susceptability to pancreatitis may lie in the fact that biliary pathology, infection, and stasis may predispose to inflammatory processes in the pancreas which are known to activate steapsinogen in the absence of the bile activator,

and thus lead to fat necrosis. That the latter may be present without pancreatitis suggests that actual presence of bile in the pancreatic ducts occurs, which conceiveably might also be favored in obesity.

Miscellaneous In connection with the less prominent digestive complications some of which have also been mentioned previously, both constipation and appendicitis have been suggested as complications favored by obesity. Axtell (7) states that the venous and portal stasis which is found in obesity may even produce splenomegaly, abdominal tympanitis enteritis, intestinal hemorrhage and even appendicitis, the latter of which he points out being common among obese. He does not believe that an obese person ever develops all this pathology, but is nevertheless more or less subject to it. Obesity is usually not regarded as a factor in either constipation or appendicitis though it is conceiveable that decreased bile secretion and sedentary habits of the obesity might operate as factors in the former, whereas a low residue (high meat) diet might favor stagnation in the appendix. Hurry(55) suggests impaired peristalsis and activity, with slowing of intestinal contents and better absorption, as a factor in the constipation of obesity. Axtell (7) in-

dicates a tendency to alternating constipation and diarrhea from acholia, while Dunlop and Lyon (38) find no higher incidence of the former in obese patients. Evidently, obesity per se has little to do with these conditions.

Love and Christie (67) however, indicate that diverticulitis of the colon from fatty infiltration of the bowel wall with consequent weakness and subsequent hernial protrusion of the mucosa may be favored by obesity. In this way obesity could indirectly promote constipation. It is further conceiveable that hemorrhoids, which have been indicated as a complication in obesity by Axtell (7) and Hurry (55) on the basis of portal stasis from heart impairment or fat deposits in the abdomen, might also favor constipation. These writers also point out the frequency of varicocele and more generalized varicosities in obesity on the same basis of general or portal stasis. Axtell indicates that portal congestion and masses of pelvic fat may impair the pelvic organs in the female obese, a consideration of which will now be undertaken.

Genito-Urinary

Renal As regards the genito-urinary tract, Beall (13) points to the parasitic nature of fat which

causes the kidneys to suffer most because of the additional burden of excretory products. It has been indicated previously however, that the role of obesity in chronic nephritis is rather remote and at worst functions only as an indirect factor.

Genital The generative organs of the obese female on the other hand, according to Axtell (7), may be so impaired functionally by venous stasis that disturbed menstruation, congestion of the ovary, and displacement and congestion of the uterus can be factors in sterility with altered endocrine imbalance. He indicates that imperfect perineal musculature in the obese may cause soft part dystocia which is often associated with infantile pelves, the latter occuring only as the result of a cause in common with the obesity. Porter(98) has observed in his practice that stout women have frequent dystocia and a tendency toward uterine inertia and exhaustion during labor. He points out that the obese female almost invaribly goes past term, apparently because of some disturbance in the normal stimulus for labor to commence. As a consequence he indicates that stout women usually have large babies which are sometimes still born necessitating induction of labor in the interest of both mother and child. He adds that diet is

good prophylaxis. It is generally accepted that the basal metabolism is increased during the latter months of pregnancy and Wyant (126) finds a slight progressive increase of the specific dynamic action with fat during the course of pregnancy which is not observed with protein or carbohydrate. It might be interesting to observe if this obtains in obese pregnant females also.

Master and Oppenheimer (76) state that in obesity menstrual difficulties, even complete amenorrhea, sterility, and sexual impotence are not uncommon. Hurry (55) states that the sexual appetite is lowered in the obese and leads to inertia of the genitalia which further predisposes to fat. There is little in the literature regarding the role of obesity in menstrual or sexual disturbances. An article entitled "Amenorrhea Due to Obesity" by F. Barach[1] was found, but not translated. Endocrine obesities could conceiveably affect the menstrual cycle or libido but it seems doubtful if obesity per se is a direct factor in these disturbances.

Meaker (83) states that the same metabolic depression which causes the obesity is likely also to induce deficient gametogenesis, amenorrhea, and steril-

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1. Wien. med. Wchnschr., 80:253, Feb.8, 1930.

ity. In regard to the latter he thinks it is a fundamental error to consider obesity as a cause of sterility. Love and Christie (67) however, state that sterility without other cause is not uncommon in the overnourished and point out that weight reduction is more important than insufflation of the fallopian tubes in effecting a cure. On the other hand, Parkes and Drummond (95) state that the result of feeding and fattening rats produces a negligable effect on the estrus cycle and no impairment in fertility. They indicate that fatness is more often a result than a cause of sterility. Heyd (53) indicates that obese females frequently have fibromyomata as well as colloid goiter, but that these are parallels rather than results of the metabolic defect of obesity.

Neuro-Muscular

Von Noorden (117) recognized that reduction cures were beneficial in certain forms of sciatica and other neuralgias. He stated that supra-orbital, occipital, and brachial forms were all relieved by reduction. He added that even hysterical obese patients were helped by the same treatment. Buck (25) suggested that metabolic wastes in obesity caused nervousness, rheumatic and neuralgic pains. Axtell (7) and Hurry (55)

indicate that somnolence is favored by obesity and vice versa due to lowered excretion of carbon dioxide, the former stressing the factors of gastro-intestinal disturbance, venous engorgement of the brain, or endocrine incompetency, while the latter adds asthenia, giddiness, and tinnitus as additional nervous complications. Additional factors in nervous and muscular complications will be indicated later in connection with other associated pathology in obesity.

Respiratory

Infectious Von Noorden (117) indicated that chronic pulmonary disease was an important complication in obesity. He enumerated chronic bronchitis, tuberculosis, kyphoscoliosis, emphysema, and adhesive pleurisy. He pointed out that the frequency of bronchitis in the obese was due to an interference with respiratory excursion of the lungs because of fat in the thorax. Hurry (55) also indicates that fat in the mediastinum, heart, ribs, and abdomen prevents expansion of the chest and respiratory movements of the lungs leading to shallower respiration. He indicates, as a consequence of raising the intra-thoracic pressure, that not only is the return of venous blood to the heart impaired, but also reduction in the oxidation occurs resulting in a possible anem-

ia from lessened amount of hemoglobin. He points out that the impaired movement and aeration of the lungs increases the liability to bronchial catarrh which tends to become chronic. He adds that the associated cough is ineffective in expelling secretions with resulting chronicity and emphysema. Axtell (7) suggests that the enfeebled heart of obesity induces congestion of the lesser circulation and so makes for predisposition to bronchitis, asthma, emphysema, pulmonary edema, severity of pneumonia and tuberculosis. He also points out that since obese have proportionally less surface area, this also contributes to lessened oxidation which makes them less able to endure exercise.

Dermal Hurry (55) indicates that an increase in panniculus also decreases heat loss which not only makes fevers more perilous in the obese, but predisposes to excessive perspiration during exercise and thus causes maceration of the skin and tendency to vulvitis and excoriation of the nymphae in females. Dearborn (31) indicates that obesity tends to inefficiency and discomfort of the skin in hot weather. Hunter (54) states that besides predisposition to diabetes and possibly hyperpiesia, the obese have a tendency to bronchitis and excessive sweating. McLester (80) states that obesity

limits comfort and increases the tendency to perspiration and eczema, as well as colds and bronchitis due to poor circulation in the panniculus adiposus. He and Beall (13) both indicate that fat is a handicap in infectious disease.

Vital Capacity Bowen and Platt (22) state that they studied the vital capacity in obesity on the basis of the following adopted normal standards based on either height or surface area:

V.C.= Ht. in cm. x 25 cc.(males) or x 20cc.(females); or

V.C.= S.A. in sq.M. x 2.5 L.(males) or x 2.0 L.(females)

They conclude that the vital capacity of obese persons up to age 50 is slightly less than normal using the height standard, and averages 20% less with the surface area standard. They add that the tendency to dyspnea in overweight people can be accounted for in part by a reduction in the vital capacity. They state that after age 50, a gradual fall in the vital capacity is normal. Buck (25) points out that excessive fat deposits in the obese not only restrict the heart in the thorax, but also the diaphragm from the abdominal side and thus lessens oxygenation of the blood. As has been previously indicated, Master and Oppenheimer (76) by roentgen-ray study note the presence of sthenic habitus and an elevated diaphragm in obese patients.

In addition to others already mentioned, Barker (9), DuBray (37), and Kisch (62) note high diaphragms in obesity, which would seem to indicate that this fact might explain the reduction in vital capacity noted above. Dearborn (31) it has been pointed out, indicates an unusual smallness of the lungs to explain the persistence of obesity. Whether or not the heightening of the diaphragm is entirely secondary to abdominal fat deposits or an inherent tendency of certain body types is difficult to determine.

Anemic McLester's (82) sthenic plethoric type does not fit in with the X-ray findings of Master and Oppenheimer above, since with their picture of sthenia and heightened diaphragm it would seem logical to expect an anemic rather than a plethoric condition, if reduced respiratory movements actually decrease aeration of the lungs and the amount of hemoglobin in the blood. It seems doubtful that uncomplicated obesity could produce a real anemia except possibly by crowding the blood forming marrow with fat, decreasing the red cell count by an obstructive liver jaundice due to fibrosis or degeneration of the hepatic cells so that they could no longer excrete bile pigments, or deficient liver storage and excretion of the

stroma-forming "X" substance secreted by the gastric mucosa. And although an anemia may cause dyspnea, it seems best to consider that reduction in vital capacity, together with increased work of the various organs best explains this symptom in obesity. The vital capacity is also reduced in such conditions as tuberculosis, pulmonary edema, emphysema, hypertrophy of the liver and heart disease all of which have been said to be associated with obesity, in which it seems to occur mainly because of encroachment of fat against the diaphragm. Bronchitis, emphysema, pneumonia, asthma, and pulmonary edema are causes of anoxic anoxemia due to impairment of the lung surfaces or capillary supply, whereas stasis of blood present in cardiac complications produces a stagnant anoxemia. Any tendency to deficient oxygenation in obesity might well be compensated for by a polycytemia, as well as dyspnea and acceleration of the heart to get rid of accumulated carbon dioxide of the blood. This might explain the plethoric tendency of some obese individuals and why they eventually suffer from the results of such a vicious circle.

Anesthetic As has already been indicated, obese patients because of impaired respiratory function, withstand infectious diseases and especially pneumonia

very poorly. Heyd (53) and others have emphasized that inhalation anesthesia is contraindicated in surgery for the obese. He points however, to the fact that impaired liver function, together with the difference between the gross or total body weight and the estimated normal or functional weight, should be considered not only in the choice of anesthesia, but in the calculation of a safe dosage. He indicates that intradural spinal block should be the first choice for the obese surgical subject. He adds that since the amount of insensible water loss varies directly with the surface area, the obese patient requires an added intake to offset the increased amount of water lost by radiation. He points out however, that poor myocardial tone contraindicates the administration of gross quantities of water to the obese.

Mechanical

Operative Love and Christie (67) point to the mechanical difficulties in operations on obese patients as well as the slowness of healing from oozing fat with the resultant prolonged convalescence and tendency to postoperative pulmonary complications. Besides these and anesthetic difficulties also, they add that obesity is a factor in obscuring both physical and X-ray

diagnosis. They suggest slow dietary reduction as the best postoperative prophylaxis. DuBray (37) states that postoperatively the obese are prone to infection, slow healing, and fat embolism and advises against local anesthesia because of the danger of fat necrosis. He also suggests preoperative dietary reduction in weight and the importance of preventing pulmonary complications, cardiac failure, wound infection, fat embolism, and hernia in the obese patient.

Hernial DuBray (37) and McLester (80) indicate the frequency of ventral hernia in obesity. Love and Christie (67) point out that the weakness resulting from the fatty infiltration of muscles impairs their efficiency and predisposes to hernia at points of greatest strain in obesity. They mention more especially the direct or acquired type of inguinal hernia, and the umbilical hernia of extra-peritoneal fat through a stretched and weakened linea alba which is eventually followed by the peritoneum. They state that the enlargement of herniae in obesity is progressive because of increased intraabdominal pressure from fat deposition in the omentum and mesentery. The frequency of ventral postoperative hernia in obese patients needs no comment.

Static

Orthopedic In addition to the mechanical complications of obesity, the effects of excessive weight bearing are of extreme seriousness. Hurry (55) states that advanced weight causes an increased effort of the sacral and lumbar muscles so that maintainance of an erect posture produces backache resulting in a tendency toward indolence which in turn aggravates the obesity. He indicates that sprains, muscular stiffness, flat feet, and grating painful knee joints are also complications of obesity. Axtell (7) states that muscular deposits of fat are a source of painful, slow, and difficult activity which explain why the obese are stiff, rheumatic and inactive. DuBray (37) points out that postural and static difficulties in the obese are due to faulty body mechanics. He includes lumbo-sacral strain and lumbago due to large heavy abdominal viscera which produce a lordosis and bilateral dull ache not involving the thighs; and sciatic scoliosis due to an asymmetrical backward inclination of the top of the pelvis which causes the lateral curvature. He adds that flat feet are common from the excessive weight bearing and flabby muscles of obesity. Love and Christie (67) also state that obese have a lordosis to compensate for a

pendulous abdomen which puts excessive strain on the sacro-iliac joints and thus causes osteo-arthritis in the hips and knees. They indicate that this as well as flat feet is precipitated by the excessive weight carrying.

Another orthopedic complication is indicated by Kirmisson (61) who states that the frequent development of coxa vara associated with obesity is more than a coincidence since it seems to be familial. He states that abortive coxalgia is another tendency in the same line and that obesity seems to be the connecting link between both affections. He adds that the obesity observed in these conditions is the type suggestive of thyrogenous origin and that radioscopy shows no abnormality in the pituitary region. Femoral neck fracture, ricketts, bone softening in adults, and senile osteo-arthritis with atrophy and bone weakness are the usual accepted causes of coxa vara, but it is conceiveable from the above how obesity may contribute to its development.

Arthritis DuBray (37) indicates that obesity usually predisposes to the hypertrophic or degenerative type of chronic arthritis (osteo-arthritis) and causes disability in this condition by mechanical irritation of bony spurs. He points out that this arthritis is more

especially of spinal location in obesity and is associated with low back pain. Parsons (96) states that faulty body mechanics is a contributing factor in the etiology of chronic arthritis. He points out that a thin ptotic type of individual is characteristic of the atrophic (infectious) arthritis, whereas hypertrophic or osteo-arthritis is more common in well nourished individuals. As has been noted earlier, Bruger and Poindexter (24) state that the plasma cholesterol is elevated in the hypertrophic type of chronic arthritis and that this elevation is more probably a result than a cause of the arthritis. Hence it would seem that obesity as a factor in arthritis is based principally on the traumatic element incident to excessive weight bearing.

In conclusion, further emphasis of the importance and variety of complications in obesity is well typified in a case presented by L.F. Barker (10). He states that the case presented multiple problems in diagnosis. The final diagnosis was diabetes, diabetic neuritis, chronic tonsillitis and sinusitis, obesity (40 lbs. overweight) with an apical systolic murmur without cardiac enlargement and a blood pressure of 155/95, allergy, hypertrophic arthritis (both hips and right knee), and postoperative ventral abdominal hernia.

SUMMARY

From a review of library material covering the literature of the past twenty years on the subject of obesity, the following facts pertaining to its causes and effects may be summarized as follows:

1. Obesity is always the result of a positive energy balance whether this be predominantly due to exogenous or endogenous factors.

2. Exogenous and endogenous factors are so intimately related that no given case may be classified as due entirely to one or the other.

3. It seems best to designate exogenous obesity as those cases where these factors predominate, ie., those due to overeating, lack of exercise, or both. That the vast majority of cases is the result of these factors is generally accepted.

4. Endogenous obesity is best applied to those cases in which pure environmental factors are in the minority and where the persistance of a positive nutritive balance seems related to more obscure internal disturbance. This class includes heredity, endocrinopathy,

and central nervous system disturbance which factors probably control body weight by influencing the appetite, feeling of satiety, and bodily activity through some interrelated mechanism of control.

5. Heredity cannot be excluded as a factor in either exogenous or endogenous obesity since it may contribute to inherent greediness or indolence as well as to body build or proportion of adipose tissue.

6. Obesity with frank stigmata of endocrinopathy or central nervous system disturbance and a lowered metabolism comprises a very small proportion of cases in which the obesity is recognized more as a symptom than a disease, though it is possible that apparent non-endocrine cases may actually be the result of hormonal or nervous disturbance so slight that obesity is the only stigma present.

7. So-called constitutional obesity is probably best classified as endogenous and in most cases is not due to lowered basal metabolism, depressed reaction to food ingestion or excercise, or anomalous transformation of metabolic products. The apparent failure of certain cases to lose weight on a subcaloric intake is best explained by the instability of the body water level, since the oxidation of fat leaves behind a large

quantity of water.

8. It is important to realize that any type of obesity may be relieved by a subcaloric diet or increase of exercise, the former being the best means of reduction since small quantities of food yield a larger number of calories than can be lost by any increase of activity.

9. Cardiac impairment in obesity is largely due to adiposity of the heart and the increased demand of greater body bulk with a greater number of blood vessels, though there is probably no increase in blood plasma volume. Obesity is more apt to produce cardiac embarrassment when some organic disease of the heart is already present. The tendency toward hypertrophy, coronary sclerosis, and arrhythmia is best explained on the basis of an overburdened heart.

10. Arteriosclerosis in obesity is followed rather than preceded by a hypercholesteremia which does not therefore seem to explain the tendency to degenerative disease in the obese. The presence of hypercholesteremia in uncomplicated obesity is controversial.

11. Whether or not arteriosclerosis precedes or follows hypertension in obesity seems uncertain, but the latter is more commonly associated with adiposity

and may be compensatory to sclerosis, increased circulatory demands or some concomitant hormonal disturbance. It is not conclusive whether hypertension is a true symptom of obesity or the result of some other factor in which adiposity operates only as a predisposing cause.

12. There is considerable evidence that obesity is associated with a lowered glucose tolerance and is the most important single etiologic factor in the production of diabetes in persons with hereditary predisposition. It may be possible that both conditions are associated as the result of a common hormonal disturbance.

13. Obesity as a factor in biliary disease is probably mostly on the basis of stasis and impaired liver function in the secretion of bile salts, rather than from any existing hypercholesteremia.

14. Fatty changes in the pancreas as well as biliary stasis may account for the frequency of pancreatitis in obesity.

15. Susceptibility to respiratory disease in the obese seems to be on the basis of reduced vital capacity produced by excessive deposits of thoracic and abdominal fat. Whether the associated elevation of the

diaphragm is entirely the result of these deposits or of inherent body build is indeterminate.

16. Gynecological complications of amenorrhea, depressed libido, and sterility are probably never directly the result of obesity, but are more likely associated because of an etiologic factor common to both.

17. Renal and anemic complications in obesity are most likely only remotely related, whereas gout and obesity are more probably associated because of some common causative factor.

18. Fatty infiltration of muscles subjected to unusual mechanical strain best explains the tendency of the obese to develop herniae. This explanation also applies to the tendency for dystocia in stout women during labor.

19. The common static effects of excessive weight bearing are lumbo-sacro-iliac disease, pes planus, and chronic hypertrophic arthritis of the spine, hips, and knees, the latter of which is probably not the result of a hypercholesteremia in obesity.

20. Most of the complicating pathology of obesity is completely removed or markedly improved by dietary reduction of the body weight, but physicians must constantly supervise the dietary regime of most overweights if normal body weight is to be maintained.

BIBLIOGRAPHY

(1) Adams, F., The Genuine Works of Hippocrates, New York, William Wood & Co., 1886. (Vol. I)

(2) Adams, S.F., Obesity as a Precursor of Diabetes, J. of Nutrition, 1:339-342, Mar. 1929.

(3) Anders, J.M. and H.L. Jameson, Adiposity and Other Etiological Factors in Diabetes Mellitus, The Am. J. of the Med. Sc., 170:313-324, Sept. 1925.

(4) Aschoff, L., Lectures on Pathology, p.131, New York, P.B. Hoeber, Inc., 1924.

(5) Aubertin, C., Obesity and Hypertension, Medecine, Paris, 4:405-480, Mar. 1923. (ab; J. of the A.M.A., 80:1815, June 16, 1923.)

(6) _____ and L. Coursier, The Blood Pressure in the Obese, Presse Medicale, Paris, 30:721, Aug. 23, 1922. (ab; J. of the A.M.A., 79:1367-1368, Oct. 14, 1922.)

(7) Axtell, L.E., Obesity: Its Related Pathology, J. of the Mich. State Med. Soc., 15:226-231, May 1916.

(8) Babonneix, L. and L. Denoyelle, Obesity with Hydrocephalus, Bulletins de la Societe Medicale des Hopitaux, Paris, 46:150, Jan. 27, 1922. (ab; J. of the A.M.A., 78:1168, Apr. 15, 1922.)

(9) Barker, L.F., The Dangers of Circulatory Insufficiency in Obesity, Especially when Associated with Emphysema and Bronchitis, Internat. Clin., 4:154-164, Dec. 1928.

(10) _____, Diabetes Mellitus and Obesity with Complications, Internat. Clin., 3:26-28, Sept. 1931.

(11) Barr, D.P., Recent Advances in Endocrinology-Relation to Interpretation and Understanding of Common Symptoms, J. of the A.M.A., 105:1760-1765, Nov. 30, 1935.

(12) Bartels, E.C. and B. Blum, Water Studies in Obesity, J. of Lab. and Clin. Med., 20:401-409, Jan. 1935.

(13) Beall, K.H., The Parasitism of Fat, Tex. State J. of Med., 18:520-521, Feb. 1923.

(14) Beck, E.C., J.G. Fowler, E.C. Koenig, and B.D. Bowen, Vascular Disease in the Obese Diabetic, and in Non-Diabetics; A discussion of Arteriosclerosis as a cause of Diabetes, Ann. of Int. Med., 9:662-670, Dec. 1935.

(15) Beeler, C. and R. Fitz, Observations on Glycemia, Glysuresis and Water Excretion in Obesity, Arch. of Int. Med., 28:804-812, Dec. 1921.

(16) Bernhardt, H., New Concepts Concerning the Pathogenesis of Obesity and the Problems of Basal Metabolism, Endocrinology, 14:209-224, July-Aug. 1930.

(17) Best, C.H. and J.M. Hershey, Further Observations on the Effects of Some Component of Crude Lecithine on Depancreatized Animals, J. of Physiol., 75:49-55, May 1932.

(18) _____, J.M. Hershey, and M.E. Huntsman, Effect of Lecithine on Fat Deposition in the Liver of Normal Rat, J. of Physiol., 75:56-66, May 1932.

(19) _____ and M.E. Huntsman, Effects of Components of Lecithine upon Deposition of Fat in the Liver, J. of Physiol., 75:405-412, Aug. 1932.

(20) Bloor, W.R., Normal Fat Metabolism, Endocrinology and Metabolism (L.F. Barker, Editor), p. 183, New York, D. Appleton & Co., 1922. (Vol. III)

(21) Booth, G. and J.M. Strang, Changes in the Temperature of the Skin Following Ingestion of Food, Arch. of Int. Med., 57:533-543, Mar. 1936.

(22) Bowen, B.D. and D.I. Platt, The Relation of Age and Obesity to Vital Capacity, Arch. of Int. Med., 31:579-589, Apr. 1923.

(23) Brown, G.E. and N.M. Keith, Blood and Plasma Volume in Obesity, Arch. of Int. Med., 33:217-223, Feb. 1924.

(24) Bruger, M. and Charles A. Poindexter, Relation of the Plasma Cholesterol to Obesity and to Some of the Complicating Diseases (Diabetes Mellitus, Essential Hypertension, Osteo-Arthritis and Arteriosclerosis), Arch. of Int. Med., 53:423-434, Mar. 1934.

(25) Buck, C.L., Circulatory Disturbance in the Obese, Boston Med. and Surg. J., 175:332-336, Sept.7, 1916.

(26) Bulmer, E., The Menace of Obesity, Brit. Med. J., 1:1024-1026, June 4, 1932.

(27) Campbell, W.R., Obesity and Its Treatment, The Can. Med. Assn. J., 34:41-48, Jan. 1936.

(28) Cushing, Harvey, The Basophile Adenomas of the Pituitary Bodies and Their Clinical Manifestations (Pituitary Basophilism), Bulletin of Johns Hopkins Hospital, 50:137-195, Mar. 1932.

(29) _____, Hyperactivation of the Neurohypophysis as the Pathological Basis of Eclampsia and Other Hypertensive States, Am. J. of Path., 10:145-173, Mar. 1934.

(30) Czerny, A., Fat Tissue and Fever, Jahrbuch fur Kinderheilkunde, Berlin, 105:24, Mar. 5, 1924,(ab; J. of the A.M.A., 82:1404, Apr. 26, 1924.)

(31) Dearborn, G.V.N., Get Fat- And Die, Interstate Med. J., 24:156-160, Feb. 1917.

(32) Dorland, W.A.N., The American Illustrated Medical Dictionary, Phil. and London, W.B. Saunders Co., 1929.

(33) Dreyer, Georges, The Assessment of Physical Fitness, New York, P.B. Hoeber, Inc., 1921.

(34) Dublin, L.I. and A.J. Lotka, Length of Life, pp.99-219, New York, The Ronald Press Co., 1936.

(35) Dublin, L.I. and H.H. Marks, The Influence of Weight on Certain Causes of Death, Human Biology, 2:159-184, May 1930.

(36) DuBois, E.F., Basal Metabolism in Health and Disease, Phil., Lea & Febiger, 1936.

(37) DuBray, E.S., Comments on Body Weight in Relation to Health and Disease, Am. J. of the Med. Sc., 170:564-575, Oct. 1925.

(38) Dunlop, D.M. and R.M. Murray Lyon, A Study of 523 Cases of Obesity, Edinburgh Med. J., 38:561-577, Oct., 1931.

(39) Elsom, J.C., The Perils of Obesity, Arch. of Phys. Therapy, 9:439-443, Oct. 1928.

(40) Emerson, W.R.P. and F.A. Manny, Underweight and Overweight in Relation to Vitality, J. of the A.M.A., 93:457, Aug. 10, 1929.

(41) Faber, E.E., Case of Obesity with Arrhythmia, Ugeskrift for Laeger, Copenhagen, 84:1741, Dec. 14, 1922. (ab; J. of the A.M.A., 80:518, Feb. 17, 1923.)

(42) Foster, N.B., The Relations of Hypertension to Cardiorenal Diseases, Am. J. of the Med. Sc., 164:808-819, Dec. 1922.

(43) Gage, Homer (Sec'y), Abstract of the Proceedings of the Twenty-fifth Annual Meeting of the Association of Life Insurance Medical Directors of America, p. 415, New York, The Knickerbocker Press, 1915. (Vol. 1913-1915)

(44) Garrison, F.H., History of Medicine, Phil. and London, W.B. Saunders Co., 1924. (3rd Ed.)

(45) Gauss, H., Obesity. Its Causes, Complications, and Treatment, Colo. Med., 24:88-96, Mar. 1927.

(46) Grafe, E., Metabolic Diseases and Their Treatment, Phil., Lea & Febiger, 1933. (Translated by Margaret Galt Boise under supervision of E.F. DuBois and H.B. Richardson)

(47) Griffiths, G.M., The Laurence-Biedl Syndrome, The J. of Neurol. and Psychopath., 12:53-58, July 1931.

(48) Gurney, R., The Hereditary Factor in Obesity, Arch. of Int. Med., 57:557-561, Mar. 1936.

(49) Hagedorn, H.C., C. Holten and A. Hecht Johansen, The Pathology of Metabolism in Obesity, Arch. of Int. Med., 40:30-37, July 1927.

(50) Harrop, George A., Milk and Banana Diet for Treatment of Obesity, J. of the A.M.A., 102:2003-2005, June 16, 1934.

(51) Hartman, H.R. and D.G. Ghrist, Blood Pressure and Weight, Arch. of Int. Med., 44:877-881, Dec. 1929.

(52) Hetenyi, Geza, Experiments on Origin of Adiposity, Deutsches Arch. f. klin. Med., 179:134-141, June 11, 1936. (From the 1936 Year Book of General Medicine, Chicago, The Year Book Publishers, Inc., Nov. 13, 1936)

(53) Heyd, C.G., The Surgical Problems of the Obese and the Lean Patient, The Surg. Clin. of N.A., 16: 713-725, June 1936.

(54) Hunter, D., Obesity, The Lancet, 2:994-996, Oct. 28, 1933.

(55) Hurry, J.B., Obesity and Its Vicious Circles, Practitioner, 99:164-181, Aug. 1917.

(56) John, H.J., The Relationship of Obesity to Carbohydrate Metabolism, Am. J. of the Med. Sc., 173:184-195, Feb. 1927.

(57) _____, The Relation of Weight to Diabetes, Endocrinology, 14:282-287, July-Aug. 1930.

(58) Joslin, E.P., Arteriosclerosis and Diabetes, Ann. of Clin. Med., 5:1061-1080, June 1927.

(59) _____, Fat and the Diabetic, The New England J. of Med., 209:519-528, Sept. 14, 1933.

(60) Joslin, E.P., L.I. Dublin and H.H. Marks, Studies in Diabetes Mellitus. III. Interpretation of the Variations in Diabetes Incidence, Am. J. of the Med. Sc., 189:163-191, Feb. 1935.

(61) Kirmission, E., Coxa Vara and Obesity, Bulletin de l'Academie de Medecine, Paris, 79:183, Mar. 5,1918. (ab; J. of the A.M.A., 70:1265, Apr. 27, 1918.)

(62) Kisch, F., Pseudo-Obesity, Medizinische Klinik, Berlin, 18:1460, Nov. 12, 1922. (ab; J. of the A.M.A., 80:147, Jan. 13, 1923.)

(63) Krantz, C.I. and J.H. Means, Epinephrin Reaction in Obesity, J. of Clin. Invest., 3:565-576, Feb. 1927.

(64) _____ and J.H. Means, The Effect of Epinephrin on the Partition of Food Stuffs in Obese and Normal Individuals, J. of Clin. Invest., 4:225-233, June 1927.

(65) Krogh, A. and J. Lindhard, The Relative Value of Fat and Carbohydrate as Sources of Muscular Energy, Biochem. J., 14:290-363, July 1920.

(66) Lambie, C.G., Obesity; Aetiology and Metabolism, Med. J. of Australia, 2:769-781, Dec.7, 1935.

(67) Love, R.J.M. and W.F. Christie, The Surgical Significance of Corpulence, The Lancet, 1:1118-1119, June 2, 1928.

(68) Lusk, G., An Investigation into the Causes of the Specific Dynamic Action of Foodstuffs, J. of Biol. Chem., 20:555-617, 1915.

(69) _____, The Elements of the Science of Nutrition, Phil. and London, W.B. Saunders Co., 1928.

(70) _____, Nutrition, Clio Medica X (E.B. Krumbhaar, Editor), New York, P.B. Hoeber, Inc., 1933.

(71) Lyon, D.M., D.M. Dunlop and C.P. Stewart, Respiratory Quotient in Obese Subjects, The Biochem. J., 26:1107-1117, 1932. (Part II)

(72) MacCallum, W.G., A Textbook of Pathology, Phil. and London, W.B. Saunders Co., 1918.

(73) Mac-Dowell, A., Disordered Heart Action in the Obese, Brazil Medico, Rio de Janeiro, 33: 25, Jan. 25, 1919. (ab; J. of the A.M.A., 72:1161, Apr. 26, 1919.)

(74) Maddox, K., Dercum's Disease (Adiposis Dolorosa), The Med. J. of Australia, 2:817-818, Dec. 26, 1931.

(75) Maranon, G. and E. Bonilla, Fatal Obesity, Revue Neurologique, Paris, 27:909, Sept. 1920. (ab; J. of the A.M.A., 76:555, Feb. 19, 1921.)

(76) Master, A.M. and E.T. Oppenheimer, A Study of Obesity-Circulatory, Roentgen-Ray and Electrocardiographic Investigations, J. of the A.M.A., 92:1652-1656, May 18, 1929.

(77) Maximow, A.A., A Textbook of Histology, Phil. and London, W.B. Saunders Co., 1930.

(78) McClellan, W.S., H.J. Spencer, E.A. Falk and E.F. DuBois, A Comparison of the Thresholds of Ketosis in Diabetes, Epilepsy and Obesity, J. of Biol. Chem., 80:639-652, Dec. 1928.

(79) McCollum, E.V. and N. Simmonds, The Newer Knowledge of Nutrition, p. 45, New York, The Macmillan Co., 1925.

(80) McLester, J.S., Obesity: Its Penalties and Treatment, Southern Med. J., 21:195-199, Mar. 1928.

(81) _____, Nutrition and Diet in Health and Disease, Phil., W.B. Saunders Co., 1928.

(82) _____, The Diagnosis and Treatment of Disorders of Metabolism, New York, Oxford University Press, 1935.

(83) Meaker, S.R., Human Sterility, p. 22, Baltimore, Williams and Wilkins Co., 1934.

(84) Means, J.H., The Basal Metabolism in Obesity, Arch. of Int. Med., 17:704-710, May 1916.

(85) Metropolitan Life Insurance Co., Statistical Bulletin, 11:4-5, June 1930.

(86) _____, Statistical Bulletin, 11:1-3, Dec. 1930.

(87) Musser, J.H., Recent Studies on Fat Metabolism, Am. J. of the Med. Sc., 198:132-144, Jan. 1935.

(88) _____ and D.O. Wright, Hypertension, Obesity and Hyperglycemia, J. of the A.M.A., 101:420-425, Aug. 5, 1933.

(89) Newburgh, L.H., The Cause of Obesity, J. of the A.M.A., 97:1659-1661, Dec. 5, 1931.

(90) _____ and M.W. Johnston, Endogenous Obesity- A Misconception, Ann. of Int. Med., 3:815-825, Feb. 1930.

(91) _____, M.W. Johnston, F.H. Lashmet, and J.M. Sheldon, Further Experiences with the Measurements of Heat Production from Insensible Loss of Weight, The J. of Nutrition, 13:203-221, Feb. 10, 1937.

(92) _____ and F.H. Lashmet, Importance of Dealing Quantitatively with Water in the Study of Disease, Am. J. of the Med. Sc., 186:461-471. Oct. 1933.

(93) _____, F.H. Wiley and F.H. Lashmet, A Method for the Determination of Heat Production Over Long Periods of Time, J. of Clin. Invest., 10:703-720, Oct. 20, 1931.

(94) Ogilvie, R.F., The Islands of Langerhans in 19 Cases of Obesity, J. of Path. and Bact., 37:473-481, Nov. 1933.

(95) Parkes, A.S. and J.C. Drummond, The Relation Between Fatness and Sterility, Brit. J. of Exper. Path., 9:63-69, Apr. 1928.

(96) Parsons, J.C., Symposium on Arthritis, J. of Iowa State Med. Soc., 25:61-65, Feb. 1935.

(97) Pedrazzini, F., Obesity and High Blood Pressure, Presse Medicale, Paris, 30:943-944, Nov. 1, 1922. (ab; J. of the A.M.A., 79:2122, Dec. 16, 1922.)

(98) Porter, W.D., Effects of Obesity on Pregnancy and Labor, Ohio State Med. J., 13:316-317, May 1917.

(99) Poulton, E.P., Obesity, Proc. of the Royal Soc. of Med., 25:347-356, Jan. 1932.

(100) Preble, W.E., Obesity: Observations on One Thousand Cases, Boston Med. and Surg. J., 188: 617-621, Apr. 26, 1923.

(101) Proger, S.H., The Electrocardiogram in Obesity, Arch. of Int. Med., 47:64-70, Jan. 1931.

(102) Reid, W.D., The Relation of Obesity to Heart Disease, Am. Heart J., 2:311-318, Feb. 1927.

(103) Riely, L.A., Obesity and Hypertension, Southern Med. J., 22:157-161, Feb. 1929.

(104) Rony, H.R., Obesity and Leanness, Illinois Med. J., 59:302-314, Apr. 1931.

(105) _____ and A.J. Levey, Studies on Fat Metabolism 1. Fat Tolerance in Obesity, J. of Lab. and Clin. Med., 15:221-228, Dec. 1929.

(106) Russell, E.F., (Editor), Abstract of the Proceedings of the Thirty-sixth Annual Meeting of the Association of Life Insurance Medical Directors of America, p. 204, New York, The Knickerbocker Press, 1926. (Vol. XII)

(107) Silver, S. and J. Bauer, Obesity, Constitutional or Endocrine?, Am. J. of the Med. Sc., 181: 769-777, June 1931.

(108) Smith, H.L. and F.A. Willius, Adiposity of the Heart, Arch. of Int. Med., 52:911-931, Dec. 1933.

)109) _____ and F.A. Willius, Cardiac Insufficiency in Obese Individuals, J. of the Iowa State Med. Soc., 25:59-61, Feb. 1935.

(110) Smith, P.E., The Disabilities Caused by Hypophysectomy and Their Repair, J. of the A.M.A., 88:158-161, Jan. 15, 1927.

(111) Stewart, C.P., R. Gaddie and D.M. Dunlop, Fat Metabolism in Muscular Exercise, The Biochem. J., 25:733-748, 1931. (Part I)

(112) Strouse, S. and M. Dye, Studies on the Metabolism of Obesity I. The Relation Between Food Intake and Body Weight in Some Obese Persons, Arch. of Int. Med., 34:267-274, Sept. 1924.

(113) _____, C.C. Wang and M. Dye, Studies on the Metabolism of Obesity II. Basal Metabolism, Arch. of Int. Med., 34:275-281, Sept. 1924.

(114) Terry, Jr., A.H., Obesity and Hypertension, J. of the A.M.A., 81:1283-1284, Oct. 13, 1923.

(115) Thompson, K.W. and Harvey Cushing, Experimental Pituitary Basophilism, Proc. of Royal Soc. of London, 115:88-100, May 1, 1934.

(116) Tyner, J.D., The Prediabetic State; Its Relation to Obesity and to Diabetic Heredity, Am. J. of the Med. Sc., 185:704-710, May 1933.

(117) Von Noorden, Carl, Clinical Treatises on the Pathology and Therapy of Disorders of Metabolism and Nutrition. Part I. Obesity, New York, E.B. Treat & Co., 1909. (Translated by Boardman Reed)

(118) Wadd, William, Cursory Remarks on Corpulence, London, J. Callow, 1816. (3rd Ed.)

(119) Walters, Waltman, R.M. Wilder and E.J. Kepler, Suprarenal Cortical Syndrome with Presentation of Ten Cases, Ann. of Surg., 100:670-687, Oct. 1934.

(120) Wang, C.C., S. Strouse, and A.D. Saunders, Studies on the Metabolism of Obesity III. The Specific Dynamic Action of Food, Arch. of Int. Med., 34:573-583, Oct. 1924.

(121) Wang, C.C., S. Strouse and A.D. Saunders, The Metabolism of Obesity IV. The Distribution of Energy Production After Food, Arch. of Int. Med., 36:397-417, Sept. 1925.

(122) Weber, F.P., The Relation of Obesity to Diabetes Mellitus, and So-called Lipogenic Diabetes, Brit. Med. J., 1:284, Feb. 13, 1926.

(123) Wiley, F.H. and L.H. Newburgh, An Improved Method for the Determination of Water Balance, J. of Clin. Invest., 10:723-732, Oct. 20, 1931.

(124) _____ and L.H. Newburgh, The Doubtful Nature of "Luxuskonsumption", J. of Clin. Invest., 10:733-744, Oct. 20, 1931.

(125) Wilson, C.L., Adiposis Dolorosa, Am. J. of Surg., 19:485-488, Mar. 1933.

(126) Wyant, Helen, Specific Dynamic Action of Protein, Carbohydrate and Fat during Pregnancy, Master of Science Thesis, Library of the University of Neb. (College of Medicine), May 24, 1930.